

10/586494

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=> file zcaplus
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FILE COVERS 1907 - 13 Nov 2008 VOL 149 ISS 20
FILE LAST UPDATED: 12 Nov 2008 (20081112/ED)

ZCAplus now includes complete International Patent Classification (IPC) reclassification data for the second quarter of 2008.

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'OBI' IS DEFAULT SEARCH FIELD FOR 'ZCPLUS' FILE

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L36      31 SEA FILE=ZCPLUS ABB=ON   PLU=ON  THALER F?/AU
L37      287 SEA FILE=ZCPLUS ABB=ON  PLU=ON  PELLICCIARI R?/AU
L38      51 SEA FILE=ZCPLUS ABB=ON  PLU=ON  BENATTI L?/AU
L39     111 SEA FILE=ZCPLUS ABB=ON  PLU=ON  SALVATI P?/AU
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L41      7 SEA FILE=ZCPLUS ABB=ON  PLU=ON  L35 AND (L36 OR L37 OR L38 OR
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FILE 'MEDLINE' ENTERED AT 16:24:31 ON 13 NOV 2008
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L37          287 SEA FILE=ZCPLUS ABB=ON  PLU=ON  PELLICCIARI R?/AU
L38          51 SEA FILE=ZCPLUS ABB=ON  PLU=ON  BENATTI L?/AU
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FILE 'ZCPLUS' ENTERED AT 16:24:43 ON 13 NOV 2008
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PROCESSING COMPLETED FOR L45

PROCESSING COMPLETED FOR L46

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L47          34 DUP REM L45 L46 (25 DUPLICATES REMOVED)
            ANSWERS '1-20' FROM FILE ZCPLUS
            ANSWER '21' FROM FILE MEDLINE
            ANSWERS '22-32' FROM FILE BIOSIS
            ANSWERS '33-34' FROM FILE WPIX
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=> d ibib abs L47 1-20; d iall L47 21-34

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L47 ANSWER 1 OF 34 ZCPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 1
ACCESSION NUMBER:      2007:1469897 ZCPLUS Full-text
DOCUMENT NUMBER:      148:100890
TITLE:                Process for the production of 2-[4-(3- and
                      2-fluorobenzyloxy)benzylamino]propanamides (safinamide
                      and ralfinamide) of high purity by catalytic
                      hydrogenation of Schiff base intermediates and their
                      use for treating CNS disorders
INVENTOR(S):          Barbanti, Elena; Caccia, Carla; Salvati, Patricia;
                      Velardi, Francesco; Rufilli, Tiziano; Bogogna, Luigi
PATENT ASSIGNEE(S):    Newron Pharmaceuticals S.p.A., Italy
SOURCE:               PCT Int. Appl., 77pp.
CODEN:                PIXXD2
DOCUMENT TYPE:        Patent
LANGUAGE:             English
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FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007147491	A1	20071227	WO 2007-EP5105	20070608
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: EP 2006-12565 A 20060619

OTHER SOURCE(S): CASREACT 148:100890; MARPAT 148:100890

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention is related to a process for preparation of therapeutically active 2-[4-(3- and 2-fluorobenzyl)benzylamino]propanamides I (safinamide (3-F) and ralfinamide (2-F)) and their pharmaceutically acceptable salts with high purity, in particular, with a content of dibenzyl derivative impurities II <0.03 weight %, preferably <0.01 weight %, via catalytic hydrogenation of the corresponding Schiff base intermediates III in the presence of a heterogeneous catalyst in a protic organic solvent. For example, α -aminoamides I and their pharmaceutically acceptable salts were prepared by fluorobenzylation of hydroxybenzaldehydes with fluorobenzyl derivs. IV [Y = Cl, Br, I, OSO₂Me, OSO₂C₆H₄-p-Me] using phase transfer catalysts, iminoalkylation of the benzaldehydes with L-alaninamide in a protic organic solvent, catalytic hydrogenation of Schiff base intermediates III in the presence of a heterogeneous catalyst in a protic organic solvent and acidulation of I with a pharmaceutically acceptable acid. Thus, fluorobenzylation of 4-hydroxybenzaldehyde with 2-fluorobenzyl chloride in toluene in the presence of potassium carbonate and tetradecyltrimethylammonium bromide gave 4-[(2-fluorobenzyl)oxy]benzaldehyde (V) which was recrystd. from diisopropyl ether gave V and a content of 3-(2-fluorobenzyl)-4-[(2-fluorobenzyl)oxy]benzaldehyde of 0.005 weight %. Iminoalkylation of fluorobenzylbenzaldehyde V with L-alaninamide hydrochloride in MeOH in the presence of TEA gave Schiff base III (2-F) which was hydrogenated in the presence of wet (50% H₂O) Pt/C at 5 bars and 35° gave ralfinamide in 93% yield with a content of (S)-2-[(3-(2-fluorobenzyl)-4-[(2-fluorobenzyl)oxy]benzyl)amino]propanamide of 0.02 weight %. Ralfinamide methanesulfonate (preparation given) containing 0.05 % dibenzylated impurity II (2-F) was tested in a cytotoxicity assay in human neuroblastoma cell line SH-SY-5Y, in a HERG current inhibition assay in transfected CHO cell lines and in a maximal electroshock test in mice and compared to II and to methanesulfonate containing II 0.3 %. As the amount of II present in ralfinamide increases, so do the undesirable features, such as cellular toxicity, strong inhibition of Cytochrome P 450, HERG channel blockage, and no protective activity in the in vivo model of epilepsy.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS

L47 ANSWER 2 OF 34 ZCPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 2
 ACCESSION NUMBER: 2007:1454651 ZCPLUS Full-text
 DOCUMENT NUMBER: 148:45877
 TITLE: Alpha-aminoamide derivatives useful in the treatment
 of cognitive disorders
 INVENTOR(S): Salvati, Patricia; Rossetti, Stefano; Benatti, Luca
 PATENT ASSIGNEE(S): Newron Pharmaceuticals S.p.A., Italy
 SOURCE: PCT Int. Appl., 38pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007144153	A2	20071221	WO 2007-EP5197	20070613
WO 2007144153	A3	20080313		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
EP 1870097	A1	20071226	EP 2006-12352	20060615
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				

PRIORITY APPLN. INFO.: EP 2006-12352 A 20060615

OTHER SOURCE(S): MARPAT 148:45877

AB The present invention is in the field of pharmacotherapy of cognitive deficits in learning and memory by administering an α -aminoamide, particularly safinamide. Examples of disturbances in cognition that can be treated with compds. of the invention are the ones associated with disorders such as autism, dyslexia, attention deficit hyperactivity disorder, schizophrenia, obsessive compulsive disorders, psychosis, bipolar disorders, depression, Tourette's syndrome, Mild Cognitive Impairment (MCI) and disorders of learning in children, adolescents and adults, Age Associated Memory Impairment, Age Associated Cognitive Decline, Alzheimer's Disease, Parkinson's Disease, Down's Syndrome, traumatic brain injury Huntington's Disease, Progressive Supranuclear Palsy (PSP), HIV, stroke, vascular diseases, Pick's or Creutzfeldt- Jacob diseases, multiple sclerosis (MS), other white matter disorders and drug-induced cognitive worsening.

L47 ANSWER 3 OF 34 ZCPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 3
 ACCESSION NUMBER: 2007:703897 ZCPLUS Full-text
 DOCUMENT NUMBER: 147:95557
 TITLE: Preparation of 2-phenylethylamino derivatives as
 calcium and/or sodium channel modulators for treating
 various diseases
 INVENTOR(S): Thaler, Florian; Napoletano, Mauro; Sabido-David,

Cibele; Moriggi, Ermanno; Caccia, Carla; Faravelli, Laura; Restivo, Alessandra; Salvati, Patricia

PATENT ASSIGNEE(S) : Newron Pharmaceuticals S.p.A., Italy

SOURCE: PCT Int. Appl., 115pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English

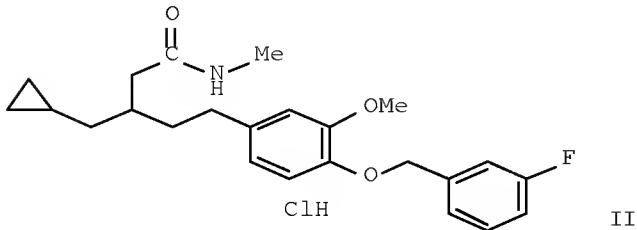
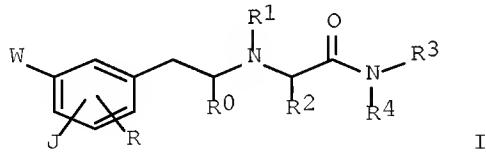
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007071311	A1	20070628	WO 2006-EP11443	20061129
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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2006329040	A1	20070628	AU 2006-329040	20061129
AU 2006329040	A2	20080605		
CA 2629065	A1	20070628	CA 2006-2629065	20061129
EP 1963280	A1	20080903	EP 2006-829177	20061129
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS				
MX 200807916	A	20080630	MX 2008-7916	20080618
KR 2008081188	A	20080908	KR 2008-718027	20080722
PRIORITY APPLN. INFO.:			EP 2005-28147	A 20051222
			WO 2006-EP11443	W 20061129

OTHER SOURCE(S) : MARPAT 147:95557

GI



AB 2-Phenylethylamino substituted carboxamide derivs. of formula I [wherein J = H or A-[$(CH_2)_n-O$]r- : n = 0 or 1; and r = 0 or 1; A = CF₃; cyclopentyl; Ph optionally substituted with a halo group, etc.; W = H, (C₁-C₄)alkoxy, etc. ; R = H or F; R₀ = H or (C₁-C₂)alkyl; R₁ = H, (C₁-C₄)alkyl optionally substituted with OH, cyclopropylmethyl, etc.; R₂ = H; (C₁-C₄)alkyl; or phenyl; R₃ = H or (C₁-C₄)alkyl; and R₄ = H; (C₁-C₄)alkyl optionally substituted; or R₃ and R₄, taken together with the adjacent N, form a pyrrolidinyl, morpholinyl or piperazinyl ring optionally substituted] and pharmaceutically acceptable salts thereof, pharmaceutical compns. containing them as active ingredient and their use as sodium and/or calcium channel modulators useful in preventing alleviating and curing a wide range of pathologies, including neurol., psychiatric, cardiovascular, inflammatory, ophthalmic, urol., and gastrointestinal diseases are described. Example compound II, prepared by reacting 2-[2-[4-(3-Fluorobenzoyloxy)-3-methoxyphenyl]ethylamino]-N-methylacetamide with the appropriate aldehyde, had an IC₅₀ of 2.1 μ M in an N-type calcium channel influx assay.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 4 OF 34 ZCAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 4

ACCESSION NUMBER: 2006:1033682 ZCAPLUS Full-text

DOCUMENT NUMBER: 145:397367

TITLE: Preparation of substituted aminoalkyl- and amidoalkyl-benzopyran derivatives as selective and reversible MAO-B inhibitors

INVENTOR(S): Carotti, Angelo; Melloni, Piero; Thaler, Florian; Caccia, Carla; Maestroni, Sara; Salvati, Patricia

PATENT ASSIGNEE(S): Newron Pharmaceuticals S.p.A., Italy

SOURCE: PCT Int. Appl., 52pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

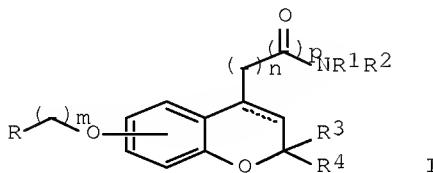
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006102958	A1	20061005	WO 2006-EP1572	20060222
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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AU 2006228787	A2	20061005	AU 2006-228787	20060222
AU 2006228787	A1	20061005		
CA 2601126	A1	20061005	CA 2006-2601126	20060222
EP 1863784	A1	20071212	EP 2006-723075	20060222
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JP 2008535824	T	20080904	JP 2008-503383	20060222
IN 2007KN02858	A	20070907	IN 2007-KN2858	20070806
CN 101137638	A	20080305	CN 2006-80008003	20070912

MX 200711832	A	20071122	MX 2007-11832	20070925
NO 2007005409	A	20071023	NO 2007-5409	20071023
KR 2007121028	A	20071226	KR 2007-724944	20071029
PRIORITY APPLN. INFO.:			EP 2005-6752	A 20050329
			WO 2006-EP1572	W 20060222

OTHER SOURCE(S): MARPAT 145:397367
GI



AB Title compds. represented by the formula I [wherein R = (un)substituted (hetero)aryl; R1, R2 = independently H, (phenyl)alkyl, (amino)alkyl, etc., or R1R2 = (un)substituted heterocyclyl; R3 = R4 = H or R3R4 = O, with proviso; m = 0-3; n = 1-3; p = 0 or 1; and pharmaceutically acceptable salts or prodrugs thereof] were prepared as selective and reversible MAO-B inhibitors. For example, Boc-deprotection of 4-[(tert-butoxycarbonylhydrazinocarbonyl)methyl]-7-benzyloxy-2H-chromen-2-one gave 4-[(hydrazinocarbonyl)methyl]-7-benzyloxy-2H-chromen-2-one (II) in 93% yield. II showed inhibition with IC₅₀ values of 1.4 μM to MAO-A and 0.04 μM to MAO-B. Thus, I and their pharmaceutical compns. are useful as MAO-B inhibitors in vitro and in vivo for the prevention and treatment of CNS degenerative disorders (no data).

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 5 OF 34 ZCPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 5

ACCESSION NUMBER: 2006:240558 ZCPLUS Full-text

DOCUMENT NUMBER: 144:286223

TITLE: Use of (halobenzyloxy)benzylaminopropanamides for the manufacture of medicaments active as sodium and/or calcium channel selective modulators

INVENTOR(S): Barbanti, Elena; Thaler, Florian; Caccia, Carla; Fariello, Ruggero; Salvati, Patricia

PATENT ASSIGNEE(S): Newron Pharmaceuticals S.p.A., Italy

SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006027052	A2	20060316	WO 2005-EP8200	20050728
WO 2006027052	A3	20060526		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,				

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AU 2005282028	A2 20060316	AU 2005-282028	20050728
AU 2005282028	A1 20060316		
CA 2577408	A1 20060316	CA 2005-2577408	20050728
EP 1809271	A2 20070725	EP 2005-769799	20050728
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CN 101018546	A 20070815	CN 2005-80030381	20050728
JP 2008512405	T 20080424	JP 2007-530600	20050728
BR 2005015154	A 20080708	BR 2005-15154	20050728
MX 200702713	A 20070523	MX 2007-2713	20070306
US 20080096965	A1 20080424	US 2007-574751	20070306
IN 2007KN00955	A 20070713	IN 2007-KN955	20070319
NO 2007001792	A 20070611	NO 2007-1792	20070404
KR 2007061863	A 20070614	KR 2007-708185	20070410
PRIORITY APPLN. INFO.:		EP 2004-21525	A 20040910
		WO 2005-EP8200	W 20050728

OTHER SOURCE(S): MARPAT 144:286223

AB The invention discloses the use of selected (R) -2- [(halobenzyloxy)benzylamino]propanamides, and pharmaceutically acceptable salts thereof, for the manufacture of medicaments that are selectively active as sodium and/or calcium channel modulators and therefore useful in preventing, alleviating and curing a wide range of pathologies, including pain, migraine, peripheral diseases, cardiovascular diseases, inflammatory processes affecting all body systems, disorders affecting skin and related tissues, disorders of the respiratory system, disorders of the immune and endocrinol. systems, gastrointestinal, urogenital, metabolic and seizure disorders, where the above mechanisms have been described as playing a pathol. role. Compound preparation is included.

L47 ANSWER 6 OF 34 ZCPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 6

ACCESSION NUMBER: 2005:177883 ZCPLUS Full-text

DOCUMENT NUMBER: 142:254593

TITLE: α -Aminoamide derivatives useful as antiinflammatory agents

INVENTOR(S): Salvati, Patricia; Veneroni, Orietta; Barbanti, Elena; Ruggero, Fariello; Benatti, Luca

PATENT ASSIGNEE(S): Newron Pharmaceuticals, SPA, Italy

SOURCE: PCT Int. Appl., 27 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005018627	A1 20050303	WO 2004-IB1574	20040422	
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,				

NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,				
TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,				
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,				
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,				
SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,				
TD, TG				
AU 2004266494	A1	20050303	AU 2004-266494	20040422
CA 2536764	A1	20050303	CA 2004-2536764	20040422
EP 1658062	A1	20060524	EP 2004-728870	20040422
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				
IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN 1842328	A	20061004	CN 2004-80024275	20040422
BR 2004013982	A	20061107	BR 2004-13982	20040422
JP 2007503424	T	20070222	JP 2006-524432	20040422
IN 2006DN00838	A	20070810	IN 2006-DN838	20060217
NO 2006000896	A	20060309	NO 2006-896	20060223
MX 2006PA02189	A	20061110	MX 2006-PA2189	20060223
US 20070276046	A1	20071129	US 2006-569403	20061218
PRIORITY APPLN. INFO.:			US 2003-497722P	P 20030825
			WO 2004-IB1574	W 20040422

OTHER SOURCE(S): MARPAT 142:254593

AB The invention discloses methods of using certain α -aminoamide derivs. as antiinflammatory agents. The antiinflammatory agents of the invention are able to reduce or even stop inflammatory conditions substantially without side effects. Compds. of the invention include e.g. (S)-(+)-2-[4-(2-fluorobenzoyloxy)benzylamino]propanamide.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 7 OF 34 ZCPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 7
 ACCESSION NUMBER: 2005:1145999 ZCPLUS Full-text
 DOCUMENT NUMBER: 143:416265
 TITLE: Alpha-aminoamide derivatives useful in the treatment of restless legs syndrome and addictive disorders
 INVENTOR(S): Besana, Claudia; Barbanti, Elena; Izzo, Emanuela; Thaler, Florian; Fariello, Ruggero; Salvati, Patricia; Benatti, Luca
 PATENT ASSIGNEE(S): Newron Pharmaceuticals S.P.A., Italy
 SOURCE: Eur. Pat. Appl., 17 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1588704	A1	20051026	EP 2004-9532	20040422
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
AU 2005235428	A1	20051103	AU 2005-235428	20050419
CA 2563674	A1	20051103	CA 2005-2563674	20050419
WO 2005102300	A1	20051103	WO 2005-EP4166	20050419
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,				

ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
 EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
 RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
 MR, NE, SN, TD, TG
 EP 1737438 A1 20070103 EP 2005-736365 20050419
 EP 1737438 B1 20080820
 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
 IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BA, HR, YU
 CN 1942179 A 20070404 CN 2005-80011890 20050419
 BR 2005009976 A 20071016 BR 2005-9976 20050419
 JP 2007533691 T 20071122 JP 2007-508825 20050419
 EP 1900362 A2 20080319 EP 2007-22078 20050419
 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
 IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BA, HR, YU
 AT 405256 T 20080915 AT 2005-736365 20050419
 IN 2006DN06080 A 20070831 IN 2006-DN6080 20061018
 NO 2006004732 A 20061122 NO 2006-4732 20061019
 MX 2006PA12163 A 20070117 MX 2006-PA12163 20061019
 KR 2007042914 A 20070424 KR 2006-721748 20061019
 US 20070203182 A1 20070830 US 2006-578988 20061219
 PRIORITY APPLN. INFO.: EP 2004-9532 A 20040422
 EP 2005-736365 A3 20050419
 WO 2005-EP4166 W 20050419

OTHER SOURCE(S): MARPAT 143:416265

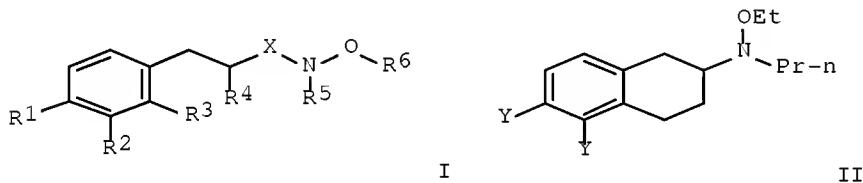
AB Methods of using certain α -aminoamide derivs. in the treatment of RLS and addictive disorders. The compds. of this invention are able to reduce or even stop the symptoms of RLS and addictive disorders substantially without side effects.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 8 OF 34 ZCPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 8
 ACCESSION NUMBER: 2005:516307 ZCPLUS Full-text
 DOCUMENT NUMBER: 143:43588
 TITLE: Preparation of O-alkyl hydroxylamines for the treatment of central nervous system disorders involving protein misfolding or misaggregation
 INVENTOR(S): Caccia, Carla; Girola, Laura; Kaltofen, Petra Karin; Losi, Daniele; Salvati, Patricia; Selva, Enrico; Thaler, Florian
 PATENT ASSIGNEE(S): Newron Pharmaceuticals S.P.A., Italy; Vicuron Pharmaceuticals, Inc.
 SOURCE: Eur. Pat. Appl., 18 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1541547	A1	20050615	EP 2003-28441	20031211
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AU 2004299232	A1	20050630	AU 2004-299232	20041210
CA 2548572	A1	20050630	CA 2004-2548572	20041210
WO 2005058800	A1	20050630	WO 2004-EP14077	20041210
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,				

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
 GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
 LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
 NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
 TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
 EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
 RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
 MR, NE, SN, TD, TG
 1692096 A1 20060823 EP 2004-803725 20041210
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS
 2007516251 T 20070621 JP 2006-543489 20041210
 20070049643 A1 20070301 US 2006-582141 20060705
 Y APPLN. INFO.: EP 2003-28441 A 20031211
 WO 2004-EP14077 W 20041210
 SOURCE(S): CASREACT 143:43588; MARPAT 143:43588



AB Title compds. I [$X = (\text{CH}_2)_n$; $n = 0-2$; R1, R2 = H, OH, OCH₃; R3 = H, CH₃; R4 = H, alkyl, together with R3 forms a 5 to 7-membered carbocyclic ring; R5, R6 = H, alkyl] and their pharmaceutically acceptable salts were prepared For example, HBr mediated deprotection of O,O-dimethylcatechol II ($Y = \text{OCH}_3$) afforded catechol II ($Y = \text{OH}$). Compds. I are claimed to be useful for the inhibition of spontaneous protein aggregation.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 9 OF 34 ZCPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 9

ACCESSION NUMBER: 2005:467805 ZCPLUS Full-text

DOCUMENT NUMBER: 143:7591

TITLE: Preparation of N-acyl-N'-benzylalkylenediamines as sodium and/or calcium channel modulators.

INVENTOR(S): Thaler, Florian; Sabido, David Cibele Maria;
Faravelli, Laura; Gagliardi, Stefania; Colombo, Elena;
Salvati, Patricia

PATENT ASSIGNEE(S) : Newron Pharmaceuticals S.p.A., Italy

SOURCE: Eur. Pat. Appl., 20 pp.

CODEN: EPXXDW

DOCUMENT

LANGUAGE : English

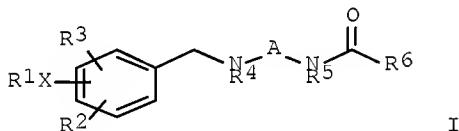
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

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EP 1535908	A1	20050601	EP 2003-27044	20031124
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AU 2004295042	A1	20050616	AU 2004-295042	20041112
CA 2546961	A1	20050616	CA 2004-2546961	20041112
WO 2005054189	A1	20050616	WO 2004-EP12834	20041112
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1689708	A1	20060816	EP 2004-803133	20041112
EP 1689708	B1	20070627		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
CN 1886370	A	20061227	CN 2004-80034601	20041112
BR 2004016914	A	20070116	BR 2004-16914	20041112
JP 2007514658	T	20070607	JP 2006-540264	20041112
AT 365713	T	20070715	AT 2004-803133	20041112
ES 2289578	T3	20080201	ES 2004-803133	20041112
MX 2006PA05776	A	20060731	MX 2006-PA5776	20060522
IN 2006DN02882	A	20070803	IN 2006-DN2882	20060522
NO 2006002350	A	20060523	NO 2006-2350	20060523
US 20070142455	A1	20070621	US 2006-580367	20060711
US 7411091	B2	20080812		
PRIORITY APPLN. INFO.:			EP 2003-27044	A 20031124
			WO 2004-EP12834	W 20041112
OTHER SOURCE(S):	CASREACT 143:7591; MARPAT 143:7591			
GI				



AB Title compds. [I; A = alkylene; X = CH₂, O, S, NR₇; R₁ = (substituted) alkyl, alkenyl, alkynyl; R₂, R₃ = H, alkyl, halo, CF₃, OH, alkoxy; R₄, R₅ = H, alkyl; R₆ = H, alkyl; R₅R₆ = atoms to form a 5-7 membered lactam ring; R₇ = H, alkyl; with a proviso], were prepared as Na and/or Ca channel modulators (no data). Thus, 1-(3-aminopropyl)pyrrolidin-2-one and 3-chloro-4-(2-fluorobenzyl)benzaldehyde (preparation given) in THF were treated dropwise with Ti(O*i*Pr)₄ in THF followed by stirring for 12 h; NaBH₄ in EtOH was added followed by heating at 70° for 6 h to give 89.4% 1-[3-[4-(2-fluorobenzyl)oxy]-3-chloroobenzylamino]propyl]pyrrolidin-2-one.

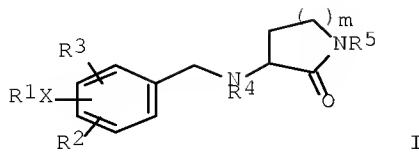
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 10 OF 34 ZCPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 10
 ACCESSION NUMBER: 2005:447060 ZCPLUS Full-text
 DOCUMENT NUMBER: 142:481942
 TITLE: Preparation of 3-benzylaminopyrrolidin-2-ones as sodium and/or calcium channel modulators.
 INVENTOR(S): Thaler, Florian; Sabido, David Cibele Maria;
 Maestroni, Sara; Raveglia, Luca Francesco; Salvati,
 Patricia
 PATENT ASSIGNEE(S): Newron Pharmaceuticals S.P.A., Italy
 SOURCE: Eur. Pat. Appl., 21 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1533298	A1	20050525	EP 2003-26779	20031121
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AU 2004295048	A1	20050616	AU 2004-295048	20041116
CA 2546653	A1	20050616	CA 2004-2546653	20041116
WO 2005054190	A1	20050616	WO 2004-EP12957	20041116
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1685103	A1	20060802	EP 2004-819593	20041116
EP 1685103	B1	20080730		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
CN 1882536	A	20061220	CN 2004-80034063	20041116
BR 2004016816	A	20070306	BR 2004-16816	20041116
JP 2007511564	T	20070510	JP 2006-540284	20041116
AT 402922	T	20080815	AT 2004-819593	20041116
IN 2006DN02725	A	20070810	IN 2006-DN2725	20060516
NO 2006002231	A	20060518	NO 2006-2231	20060518
MX 2006PA05626	A	20060817	MX 2006-PA5626	20060518
US 20070135410	A1	20070614	US 2006-579675	20060706
PRIORITY APPLN. INFO.:			EP 2003-26779	A 20031121
			WO 2004-EP12957	W 20041116

OTHER SOURCE(S): CASREACT 142:481942; MARPAT 142:481942

GI



AB Use of title compds. [I; m = 1-3; X = CH₂, O, S, NR₆; R₁ = alkyl, alkenyl, alkynyl chain, optionally substituted with CF₃, (substituted) Ph, PhO, naphthyl; R₂, R₃ = H, alkyl, halo, CF₃, OH, alkoxy; R₄-R₆ = H, alkyl] for the preparation of a drug having Na or Ca channel modulating activity is claimed (no data). Thus, (S)-3-aminopyrrolidin-2-one (preparation given) was stirred with NaBH₃CN and 3 Å mol. sieves in MeOH; 4-(3-fluorobenzyl)benzaldehyde in MeOH was added to give after 3 h 74% (S)-3-[4-(3-fluorobenzyl)benzylamino]pyrrolidin-2-one.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 11 OF 34 ZCPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 11

ACCESSION NUMBER: 2004:872683 ZCPLUS Full-text

DOCUMENT NUMBER: 141:370536

TITLE: Combination chemotherapy for treatment of parkinson's disease by using safinamides and MAO-B inhibitors together with other antiparkinsonian agents

INVENTOR(S): Ruggero, Fariello; Cattaneo, Carlo; Salvati, Patricia; Benatti, Luca

PATENT ASSIGNEE(S): Newron Pharmaceuticals, Inc., Italy

SOURCE: PCT Int. Appl., 43 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004089353	A2	20041021	WO 2004-IB1408	20040408
WO 2004089353	A3	20041216		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004228782	A1	20041021	AU 2004-228782	20040408
CA 2523188	A1	20041021	CA 2004-2523188	20040408
EP 1613296	A2	20060111	EP 2004-726590	20040408
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
BR 2004009364	A	20060425	BR 2004-9364	20040408
CN 1771030	A	20060510	CN 2004-80009655	20040408

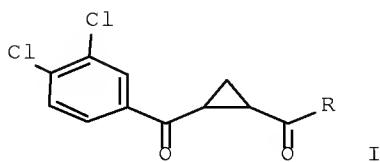
JP 2006522800	T	20061005	JP 2006-506582	20040408
NZ 542910	A	20071026	NZ 2004-542910	20040408
NO 2005004640	A	20051209	NO 2005-4640	20051010
MX 2005PA10873	A	20060321	MX 2005-PA10873	20051010
IN 2005DN04581	A	20070817	IN 2005-DN4581	20051010
US 20070093495	A1	20070426	US 2005-559982	20051209
PRIORITY APPLN. INFO.:			US 2003-462205P	P 20030411
			WO 2004-IB1408	W 20040408

AB New uses of safinamide, safinamide derivs. and MAO-B inhibitors in novel types of treatment for Parkinson's Disease are described. More specifically, the invention relates to methods for treating Parkinson's Disease through the administration of safinamide, a safinamide derivative, or a MAO-B inhibitor, in combination with other Parkinson's Disease agents or treatments, such as levodopa/PDI or dopamine agonists. For example, safinamide as an anticonvulsant was proved through clin. trials to be potent and safe to treat idiopathic early Parkinson's disease.

L47 ANSWER 12 OF 34 ZCPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 12

ACCESSION NUMBER: 2004:960074 ZCPLUS Full-text
 DOCUMENT NUMBER: 141:374741
 TITLE: Preparation of glycoside derivatives of 2-(3,4-dichlorobenzoyl)-cyclopropane-1-carboxylic acid as kynurenine 3-monooxygenase and glutamate release inhibitors
 INVENTOR(S): Benatti, Luca; Fariello, Ruggero; Salvati, Patricia; Pellicciari, Roberto; Caccia, Carla
 PATENT ASSIGNEE(S): Newron Pharmaceuticals S.P.A., Italy
 SOURCE: Eur. Pat. Appl., 10 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1475385	A1	20041110	EP 2003-10120	20030505
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRIORITY APPLN. INFO.:			EP 2003-10120	20030505
OTHER SOURCE(S):	MARPAT 141:374741			
GI				



AB Glycoside derivs. of 2-(3,4-dichlorobenzoyl)-cyclopropane-1-carboxylic acid I, wherein R is a glycoside residue optionally having one or more hydroxy groups alkylated or acylated by C1-C4 alkyl or acyl groups, were prepared as long lasting inhibitors of kynurenine 3-monooxygenase (KMO) and potent glutamate

(GLU) release inhibitors. Thus, α -D-galactopyranosyl (1S,2S)-2-(3,4-Dichlorobenzoyl)cyclopropane-1-carboxylate (II) was prepared and tested in rats as KMO and GLU release inhibitor. II inhibited in vitro brain KMO (IC₅₀ = 66 nM). When the compound was pre-incubated with mitochondria preparation for 30 min before adding the substrate kynurenone (KYN), the IC₅₀ was not significantly different. KMO activity was evaluated by measuring by HPLC the formation of 3-OH-KYN in homogenates incubated in the presence of a fixed concentration of KYN (close to the enzyme Km that in our exptl. conditions is 30 μ M). The most relevant finding is, however, the fact that II potently inhibits GLU release in the brain and this effect is still present 24 h after a single systemic administration.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 13 OF 34 ZCPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 13
 ACCESSION NUMBER: 2004:584466 ZCPLUS Full-text
 DOCUMENT NUMBER: 141:128830
 TITLE: Alpha-aminoamide derivatives useful as antimigraine agents
 INVENTOR(S): Salvati, Patricia; Calabresi, Marcello; Dho, Luciano; Veneroni, Orietta; Melloni, Piero
 PATENT ASSIGNEE(S): Newron Pharmaceuticals S.P.A., Italy
 SOURCE: Eur. Pat. Appl., 12 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1438956	A1	20040721	EP 2003-921	20030116
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CA 2510514	A1	20040729	CA 2003-2510514	20031118
WO 2004062655	A1	20040729	WO 2003-EP12889	20031118
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003279399	A1	20040810	AU 2003-279399	20031118
EP 1585510	A1	20051019	EP 2003-772344	20031118
EP 1585510	B1	20071205		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003017795	A	20051122	BR 2003-17795	20031118
CN 1738611	A	20060222	CN 2003-80108890	20031118
JP 2006514060	T	20060427	JP 2004-565939	20031118
AT 380026	T	20071215	AT 2003-772344	20031118
NZ 541117	A	20080229	NZ 2003-541117	20031118
ES 2295658	T3	20080416	ES 2003-772344	20031118
RU 2336077	C2	20081020	RU 2005-125919	20031118
US 20060079570	A1	20060413	US 2005-541195	20050630
MX 2005PA07339	A	20050930	MX 2005-PA7339	20050706

10/586494

IN 2005KN01531	A	20061027	IN 2005-KN1531	20050803
NO 2005003780	A	20051013	NO 2005-3780	20050809
PRIORITY APPLN. INFO.:			EP 2003-921	A 20030116
			WO 2003-EP12889	W 20031118

OTHER SOURCE(S): MARPAT 141:128830

AB α -Aminoamide derivs. useful as antimigraine agents, particularly for the treatment of head pain conditions such as migraine, cluster headache or other severe headache, are disclosed. The antimigraine agents of the invention are able to reduce or even stop the pain deriving from such conditions without, virtually, any side effects.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 14 OF 34 ZCPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 14

ACCESSION NUMBER: 2004:446921 ZCPLUS Full-text

DOCUMENT NUMBER: 141:7013

TITLE: Preparation of halothienoylcyclopropanecarboxylic acids as long lasting inhibitors of kynurenine 3-monooxygenase (KMO).

INVENTOR(S): Benatti, Luca; Fariello, Ruggero; Salvati, Patricia; Fellicciari, Roberto; Caccia, Carla

PATENT ASSIGNEE(S): Newron Pharmaceuticals S.P.A., Italy

SOURCE: Eur. Pat. Appl., 15 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

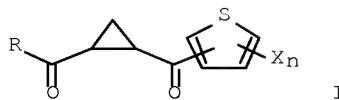
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1424333	A1	20040602	EP 2002-26597	20021128
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
CA 2507597	A1	20040610	CA 2003-2507597	20031125
WO 2004048361	A1	20040610	WO 2003-EP13244	20031125
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003296596	A1	20040618	AU 2003-296596	20031125
EP 1565451	A1	20050824	EP 2003-811772	20031125
EP 1565451	B1	20070509		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006509753	T	20060323	JP 2004-554463	20031125
AT 361921	T	20070615	AT 2003-811772	20031125
ES 2286509	T3	20071201	ES 2003-811772	20031125
US 20060116329	A1	20060601	US 2005-536307	20051227
PRIORITY APPLN. INFO.:			EP 2002-26597	A 20021128
			WO 2003-EP13244	W 20031125

OTHER SOURCE(S): MARPAT 141:7013

GI



AB Title compds. (I; R = OH, C1-6 alkoxy, PhO, PhCH₂O, NR₁R₂, glycoside residue, primary alkoxy residue from ascorbic acid, optionally having ≥1 OH groups alkylated or acylated by C1-4 alkyl, acyl; R₁ = H, alkyl, PhCH₂, Ph; R₂ = H, C1-4 alkyl; X = F, Cl, Br; n = 1, 2) are long lasting inhibitors of kynurenine 3-monooxygenase (KMO) (no data). Thus, a 2M solution of a Grignard reagent prepared from 2-chloro-4-bromothiophene in THF was added to Me trans-2-[(N-methoxy-N-methyl)aminocarbonyl]cyclopropane-1-carboxylate (preparation given) in THF at 0° followed by stirring at room temperature for 14 h to give 44% Me trans-2-(2-chloro-4-thienoyl)cyclopropane-1-carboxylate.

L47 ANSWER 15 OF 34 ZCPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 15

ACCESSION NUMBER: 2003:202474 ZCPLUS Full-text

DOCUMENT NUMBER: 138:215340

TITLE: Pharmaceutical composition comprising gabapentin or an analogue thereof and an α-aminoamide, and its analgesic use

INVENTOR(S): Salvati, Patricia; Veneroni, Orietta; Maj, Roberto; Fariello, Ruggero; Benatti, Luca

PATENT ASSIGNEE(S): Newron Pharmaceuticals S.p.A., Italy

SOURCE: PCT Int. Appl., 21 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003020273	A2	20030313	WO 2002-EP8910	20020809
WO 2003020273	A3	20030904		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1287853	A1	20030305	EP 2001-121069	20010903
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CA 2459470	A1	20030313	CA 2002-2459470	20020809
AU 2002333374	A1	20030318	AU 2002-333374	20020809
AU 2002333374	A2	20030318		
AU 2002333374	B2	20070322		
EP 1423168	A2	20040602	EP 2002-797573	20020809

EP 1423168	B1	20060208	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK			
BR 2002012298	A	20040914	BR 2002-12298 20020809
JP 200504782	T	20050217	JP 2003-524580 20020809
NZ 531586	A	20050930	NZ 2002-531586 20020809
AT 317280	T	20060215	AT 2002-797573 20020809
PT 1423168	T	20060531	PT 2002-797573 20020809
ES 2253579	T3	20060601	ES 2002-797573 20020809
RU 2295337	C2	20070320	RU 2004-110041 20020809
NO 2004000907	A	20040514	NO 2004-907 20040302
MX 2004PA02009	A	20040708	MX 2004-PA2009 20040302
IN 2004KN00432	A	20060414	IN 2004-KN432 20040331
US 20040248978	A1	20041209	US 2004-487931 20040726
HK 1070305	A1	20070420	HK 2005-102974 20050408
PRIORITY APPLN. INFO.:			EP 2001-121069 A 20010903
			WO 2002-EP8910 W 20020809

AB A pharmaceutical composition for analgesic use is disclosed which comprises gabapentin or an analog thereof (pregabalin or tiagabine) and an α -aminoamide. A synergistic effect of the resp. analgesic activities without concomitant increase of side effects was observed

L47 ANSWER 16 OF 34 ZCPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 16

ACCESSION NUMBER: 2003:166721 ZCPLUS Full-text

DOCUMENT NUMBER: 139:301785

TITLE: Anti-allodynic effect of NW-1029, a novel Na⁺ channel blocker, in experimental animal models of inflammatory and neuropathic pain

AUTHOR(S): Veneroni, C.; Maj, R.; Calabresi, M.; Faravelli, L.; Fariello, R. G.; Salvati, P.

CORPORATE SOURCE: Newron Pharmaceuticals S.p.A Research and Development, Gerenzano, Varese, Italy

SOURCE: Pain (2003), 102(1-2), 17-25
CODEN: PAINDB; ISSN: 0304-3959

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB NW-1029, a benzylamino propanamide derivative, was selected among several mols. of this chemical class on the basis of its affinity for the [3H]batracotoxin ligand displacement of the Na⁺ channel complex and also on the basis of its voltage and use-dependent inhibitory action on the Na⁺ currents of the rat DRG (dorsal root ganglia) sensory neuron. This study evaluated the analgesic activity of NW-1029 in animal models of inflammatory and neuropathic pain (formalin test in mice, complete Freund's adjuvant and chronic constriction injury in rats) as well as in acute pain test (hot-plate and tail-flick in rats). Orally administered NW-1029 dose-dependently reduced cumulative licking time in the early and late phase of the formalin test (ED50=10.1 mg/kg in the late phase). In the CFA model, NW-1029 reversed mech. allodynia (von Frey test) after both i.p. and p.o. administration (ED50=0.57 and 0.53 mg/kg), resp. Similarly, NW-1029 reversed mech. allodynia in the CCI model after both i.p. and p.o. administration yielding an ED50 of 0.89 and 0.67 mg/kg, resp. No effects were observed in the hot-plate and tail-flick tests up to 30 mg/kg p.o. The compound orally administered (0.1-10 mg/kg) was well tolerated, without signs of neurol. impairment up to high doses (ED50=470 and 245 mg/kg in rat and mice Rotarod test, resp.). These results indicate that NW-1029 has anti-nociceptive properties in models of inflammatory and neuropathic pain.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 17 OF 34 ZCPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 18
 ACCESSION NUMBER: 1998:497734 ZCPLUS Full-text
 DOCUMENT NUMBER: 129:288651
 ORIGINAL REFERENCE NO.: 129:58789a,58792a
 TITLE: Temporal and spatial changes of quinolinic acid immunoreactivity in the gerbil hippocampus following transient cerebral ischemia
 AUTHOR(S): Baratte, S.; Molinari, A.; Veneroni, O.; Speciale, C.; Benatti, L.; Salvati, P.
 CORPORATE SOURCE: CNS Research, Pharmacia and Upjohn, Nerviano, 20014, Italy
 SOURCE: Molecular Brain Research (1998), 59(1), 50-57
 CODEN: MBREE4; ISSN: 0169-328X
 PUBLISHER: Elsevier Science B.V.
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Quinolinic acid (QUIN) is an endogenous neurotoxin which originates from the kynurene pathway of tryptophan metabolism. An increase of brain QUIN level occurs in several degenerative and inflammatory disorders, but the cellular source of QUIN is still a matter of controversy. In the present study, the gerbil model of transient global ischemia was used to investigate the time course and the cellular localization of QUIN immunoreactivity. Neurodegeneration was evident in the subiculum and in the CA1 area of the hippocampus 4, 7 and 14 days after ischemia. QUIN pos. cells, with microglia-like morphol., appeared in the subiculum and in the CA1, 4 days after ischemia. At 7 days post-ischemia they extended to the whole CA1, disappearing at 14 days. Neither neurodegeneration nor QUIN pos. cells could be detected in ischemic gerbils sacrificed at 1 and 2 days after ischemia and in sham-operated animals. These findings suggest that microglia-like cells infiltrating the degenerating areas of the hippocampus represent the major source of QUIN following transient ischemia in the gerbil. Thus, *in situ* production of QUIN in vulnerable brain regions may contribute to the pathophysiol. mechanisms of delayed brain injury.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 18 OF 34 ZCPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 19
 ACCESSION NUMBER: 1995:480908 ZCPLUS Full-text
 DOCUMENT NUMBER: 122:288107
 ORIGINAL REFERENCE NO.: 122:52483a,52486a
 TITLE: Growth abnormalities in cultured mesangial cells from rats with spontaneous glomerulosclerosis
 AUTHOR(S): Pugliese, Francesco; Ferrario, Romana G.; Ciavolella, Antonella; Tamburin, Monica; Benatti, Luca; Casini, Alessandro; Patrono, Carlo; Salvati, Patricia
 CORPORATE SOURCE: Department Medicine, University Rome "La Sapienza", Milan, Italy
 SOURCE: Kidney International (1995), 47(1), 106-13
 CODEN: KDYIA5; ISSN: 0085-2538
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Age-related glomerulosclerosis (GS) occurs in normotensive rats of the Milan strain (MNS), but not in genetically-matched hypertensive animals (MHS). Altered mesangial cell (MC) proliferation and matrix expansion are common features of the glomerular scarring process. We evaluated proliferation and matrix protein synthesis of cultured MC from MNS and MHS animals aged 1 and 8 mo, i.e., before and after the occurrence of GS. [³H]-thymidine (TdR) incorporation into DNA of MC from MNS rats stimulated by 10% FBS serum increased with donor aging from 115 ± 6.0 to 176 ± 15, P < 0.01 (% cpm/well

over quiescent controls \pm SEM). Under the same exptl. conditions, cell counts changed from 101 ± 4.0 to 146 ± 5.0 , $P < 0.01$ (% cells/well over quiescent controls). Addnl., cytosolic Ca²⁺ concentration ([Ca²⁺]i) rised from 115 ± 19 to 220 ± 32 nM and from 112 ± 24 to 734 ± 136 nM when fura-2-loaded cells from young and old MNS rats, resp., were stimulated with 1% FBS. The rate of collagen production also increased with donor age, as well as collagen IV and laminin B1 mRNA expression. In contrast, in MC from MHS rats both DNA synthesis and cell replication rate declined as function of donor age. No differences in the [Ca²⁺]i responses to FBS were observed, nor collagen production changed with MHS rat senescence. We conclude that the age-associated decline of proliferative activity in MC from MHS animals could actually reflect a normal process of cell aging, possibly protecting from the occurrence of GS. At variance, in MNS rat-derived cells such physiol. process may be genetically altered. This may translate into an age-dependent hyperresponsiveness to growth stimuli, thereby facilitating the development of GS.

L47 ANSWER 19 OF 34 ZCPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2005:696729 ZCPLUS Full-text
 DOCUMENT NUMBER: 143:179626
 TITLE: Alpha-aminoamide derivatives useful in the treatment of lower urinary tract disorders
 INVENTOR(S): Barbanti, Elena; Veneroni, Orietta; Thaler, Florian; Pellicciari, Roberto; Benatti, Luca; Salvati, Patricia
 PATENT ASSIGNEE(S): Newron Pharmaceuticals S.P.A., Italy
 SOURCE: PCT Int. Appl., 42 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005070405	A1	20050804	WO 2005-EP514	20050120
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1557166	A1	20050727	EP 2004-1175	20040121
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AU 2005205903	A1	20050804	AU 2005-205903	20050120
CA 2554047	A1	20050804	CA 2005-2554047	20050120
CN 1956714	A	20070502	CN 2005-80002785	20050120
BR 2005006970	A	20070703	BR 2005-6970	20050120
JP 2007518763	T	20070712	JP 2006-550030	20050120
MX 2006PA08188	A	20061020	MX 2006-PA8188	20060719
IN 2006DN04152	A	20070810	IN 2006-DN4152	20060719
NO 2006003368	A	20061012	NO 2006-3368	20060720
KR 2007007776	A	20070116	KR 2006-714655	20060720

10/586494

US 20080132567	A1	20080605	US 2007-586494	20070125
PRIORITY APPLN. INFO.:			EP 2004-1175	A 20040121
			US 2003-497722P	P 20030825
			WO 2005-EP514	W 20050120

OTHER SOURCE(S): MARPAT 143:179626

AB The present invention discloses certain α -aminoamide derivs., a chemical class of sodium channel blockers, and their use for treating lower urinary tract disorders and to pharmaceutical compns. containing them. Compds. of the invention include e.g. 2-[(3-phenethyl-2,3-dihydro-benzofuran-5-ylmethyl)-amino]-N-methyl- propanamide. To prepare above compound, a solution of N-methyl-alaninamide hydrochloride 0.50 g in methanol 10 mL, in the presence of mol. sieves 1 g, sodium cyanoborohydride 0.36 g and a solution of 3-(2-phenylethyl)-2,3-dihydro-1-benzofuran-5-carboxaldehyde 0.90 g in methanol 10 mL were added at room temperature. The reaction mixture was kept under stirring and an argon atmospheric for 12 h. Then, the solvent was evaporated under vacuum and purified by flash chromatog. affording 0.93g of 2-[(3-phenethyl-2,3-dihydro-benzofuran-5-ylmethyl)-amino]-N-methyl- propanamide, identified by NMR.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 20 OF 34 ZCPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:634620 ZCPLUS Full-text

TITLE: TTX-sensitive and TTX-resistant sodium channels

AUTHOR(S): Salvati, Patricia; Faravelli, L.; Veneroni, O.

CORPORATE SOURCE: Newron Pharmaceuticals SpA, Bresso (MI), Italy

SOURCE: Abstracts of Papers, 226th ACS National Meeting, New York, NY, United States, September 7-11, 2003 (2003), MEDI-010. American Chemical Society: Washington, D. C.

CODEN: 69EKY9

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB Voltage gated sodium channels (VGSC) play an important role in the generation of ectopic discharges after nerve injury. Adult rat DRG neurons express six VGSC --subunits (Nav1.1, Nav1.6, Nav1.7, Nav1.8, Nav1.9 and Nav1.0) which underlie distinct sodium currents: fast TTXs, slow TTXr and persistent TTXr, based on kinetic properties and sensitivity to tetrodotoxin (TTX). The expression of Nav1.3 (TTXs), Nav1.8 (TTXr) and Nav1.9 (TTXr) channels is developmentally regulated and is altered in models of inflammatory and neuropathic pain. NW-1029 is a novel VGSC blocker with preferential inhibitory effects on TTXr currents in depolarized in vitro conditions, with long lasting anti-hyperalgesic and anti-allodynic oral activity in animal models of neuropathic and inflammatory pain. This activity is not accompanied by CNS-related side effects.

L47 ANSWER 21 OF 34 MEDLINE on STN DUPLICATE 17

ACCESSION NUMBER: 1999203305 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 10103072

TITLE: ZFM1/SF1 mRNA in rat and gerbil brain after global ischaemia.

AUTHOR: Covini N; Tamburin M; Consalez G; Salvati P; Benatti L

CORPORATE SOURCE: Pharmacia & Upjohn, CNS Research, 20014 Nerviano, Italy.

SOURCE: The European journal of neuroscience, (1999 Mar) Vol. 11, No. 3, pp. 781-7.
 Journal code: 8918110. ISSN: 0953-816X.

PUB. COUNTRY: France
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199904
 ENTRY DATE: Entered STN: 11 May 1999
 Last Updated on STN: 3 Mar 2000
 Entered Medline: 26 Apr 1999

ABSTRACT:

Cerebral ischaemia results in significant brain damage, but the molecular mechanisms associated with ischaemia-induced brain injury are not well defined. We have adopted an improved differential-display method to search for new ischaemia-related genes. Among the different cDNAs isolated following transient forebrain ischaemia in rat, PH3.3 was selected for further studies. The search for homologies revealed that it is the rat homologue to human zinc finger motif 1 (ZFM1), also called mammalian splicing factor 1 (SF1). With Northern blot, PH3.3 hybridized with three mRNA species of 2.3, 2.9 and 3.6 kb, significantly increased at 6 h and 5 days after the ischaemic insult. These findings were extended also to another animal model. In situ hybridization in ischaemic gerbils showed that PH3.3 mRNA was induced in the dentate gyrus as early as 4 h post-ischaemia. Expression peaked at 2 days in the whole hippocampus and cortex, and then progressively decreased towards sham levels. By day 4, expression had disappeared almost entirely from the cells in the CA1 region of the hippocampus, concomitant with the degeneration of pyramidal neurons. Interestingly, ZFM1/SF1 has been recently identified as activated following p53-induced apoptosis. Several lines of evidence suggest that p53 may play two roles in the post-ischaemic brain. The primary role of p53 is to activate DNA repair processes, but if repair fails, apoptosis will be initiated. Thus, ZFM1/SF1 may represent a relevant link between p53 and the neuroprotective/neurodegenerative processes which follow cerebral ischaemia.

CONTROLLED TERM: Check Tags: Male
 Amino Acid Sequence
 Animals
 Blotting, Northern
 *Brain Chemistry: PH, physiology
 *Brain Ischemia: ME, metabolism
 *Carrier Proteins: GE, genetics
 Cloning, Molecular
 DNA Probes
 *DNA-Binding Proteins
 *Dentate Gyrus: BS, blood supply
 Dentate Gyrus: CH, chemistry
 Gene Expression: PH, physiology
 Gerbillinae
 In Situ Hybridization
 Molecular Sequence Data
 *Nuclear Proteins: GE, genetics
 Polymerase Chain Reaction
 RNA Splicing: PH, physiology
 RNA, Messenger: AN, analysis
 Rats
 Rats, Wistar
 *Transcription Factors
 Tumor Suppressor Protein p53: GE, genetics
 Zinc Fingers: GE, genetics
 0 (Carrier Proteins); 0 (DNA Probes); 0 (DNA-Binding Proteins); 0 (Nuclear Proteins); 0 (RNA, Messenger); 0

CHEMICAL NAME:

10/586494

(Transcription Factors); 0 (Tumor Suppressor Protein p53);
0 (Zfp162 protein, rat)

L47 ANSWER 22 OF 34 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN

ACCESSION NUMBER: 2003:576770 BIOSIS Full-text
DOCUMENT NUMBER: PREV200300579496

TITLE: TTX-sensitive and TTX-resistant sodium channels.
AUTHOR(S): Salvati, Patricia [Reprint Author]; Faravelli, L.
[Reprint Author]; Veneroni, O. [Reprint Author]

CORPORATE SOURCE: Newron Pharmaceuticals SpA, Via L. Ariosto, 21, Bresso, MI,
Italy

SOURCE: Abstracts of Papers American Chemical Society, (2003) Vol.
226, No. 1-2, pp. MEDI 10. print.
Meeting Info.: 226th ACS (American Chemical Society)
National Meeting. New York, NY, USA. September 07-11, 2003.
American Chemical Society.
ISSN: 0065-7727 (ISSN print).

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 10 Dec 2003
Last Updated on STN: 10 Dec 2003

CONCEPT CODE: General biology - Symposia, transactions and proceedings
00520
Cytology - Animal 02506
Pathology - Therapy 12512
Nervous system - Physiology and biochemistry 20504
Nervous system - Pathology 20506
Pharmacology - General 22002
Pharmacology - Neuropharmacology 22024

INDEX TERMS: Major Concepts
Nervous System (Neural Coordination); Pharmacology

INDEX TERMS: Parts, Structures, & Systems of Organisms
DRG neurons: nervous system

INDEX TERMS: Diseases
neuropathic pain: nervous system disease
Pain (MeSH)

INDEX TERMS: Chemicals & Biochemicals
NW-1029: analgesic-drug; TTX; voltage gated sodium
channels

ORGANISM: Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
rat (common): adult
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates,
Nonhuman Mammals, Rodents, Vertebrates

REGISTRY NUMBER: 346670-96-0 (NW-1029)

L47 ANSWER 23 OF 34 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN

ACCESSION NUMBER: 2003:304410 BIOSIS Full-text
DOCUMENT NUMBER: PREV200300304410

TITLE: NW - 1029: A POTENT Na⁺ CHANNEL BLOCKER WITH
ANTIHYPERALGESIC EFFECT IN ANIMAL MODELS OF INFLAMMATORY
AND NEUROPATHIC PAIN.

AUTHOR(S): Veneroni, O. [Reprint Author]; Faravelli, L. [Reprint

Author]; Calabresi, M. [Reprint Author]; Maj, R. [Reprint Author]; Fariello, R. G. [Reprint Author]; Salvati, P. [Reprint Author]

CORPORATE SOURCE: CNS, Newron Pharmaceuticals S.p.A., Gerenzano, Varese, Italy

SOURCE: Society for Neuroscience Abstract Viewer and Itinerary Planner, (2002) Vol. 2002, pp. Abstract No. 454.3.
<http://sfn.scholarone.com>. cd-rom.

Meeting Info.: 32nd Annual Meeting of the Society for Neuroscience. Orlando, Florida, USA. November 02-07, 2002.

Society for Neuroscience.

DOCUMENT TYPE: Conference; (Meeting)
 Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 2 Jul 2003

Last Updated on STN: 2 Jul 2003

ABSTRACT: NW-1029 is a novel Na channel blocker with antihyperalgesic activity in animal models of pain. Aims of the present study were 1) to evaluate the electrophysiological properties of NW-1029 on Na currents of adult rat DRG neurons; 2) to evaluate the acute oral analgesic activity of the compound in two animal models of inflammatory (CFA) and neuropathic pain (CCI) in rats; 3) to confirm the effect on existing allodynia after chronic treatment, in order to exclude tolerance to its antihyperalgesic effect. NW-1029 displayed voltage and use dependent inhibition of PNS Na currents in a molar range of concentration. In both the CFA and CCI models orally administered NW-1029 reversed mechanical allodynia with an ED₅₀ of 0.53 and 0.67 mg/kg respectively. The effect had a quick onset and long duration (> 7 h). In the CFA model NW-1029 also reversed thermal allodynia dose dependently in a range dose of 1 to 10 mg/kg. The antinociceptive activity persisted after chronic treatment. In fact in the CCI model the ED₅₀ was 0.65 mg/kg after 10 days treatment with 1.0 mg/kg p.o. Conclusions: The results of these studies indicate that the inhibitory effect of NW-1029 on the Na currents expressed in the DRG sensory neurons accompanies a antihyperalgesic effect not associated to development of tolerance. These findings emphasize NW-1029 potential of being efficacious in man pain conditions.

CONCEPT CODE: General biology - Symposia, transactions and proceedings
 00520
 Cytology - Animal 02506
 Pathology - Therapy 12512
 Nervous system - Physiology and biochemistry 20504
 Nervous system - Pathology 20506
 Pharmacology - General 22002
 Pharmacology - Neuropharmacology 22024

INDEX TERMS: Major Concepts
 Nervous System (Neural Coordination); Pharmacology

INDEX TERMS: Parts, Structures, & Systems of Organisms
 DRG neuron: nervous system, dorsal root ganglion neuron

INDEX TERMS: Diseases
 inflammatory pain: nervous system disease

INDEX TERMS: Diseases
 neuropathic pain: nervous system disease
 Pain (MeSH)

INDEX TERMS: Chemicals & Biochemicals
 NW-1029: analgesic-drug, sodium channel blocker

INDEX TERMS: Miscellaneous Descriptors
 sodium current; thermal allodynia

ORGANISM: Classifier
 Muridae 86375
 Super Taxa
 Rodentia; Mammalia; Vertebrata; Chordata; Animalia

Organism Name

rat (common): adult, animal model

Taxa Notes

Animals, Chordates, Mammals, Nonhuman Vertebrates,
Nonhuman Mammals, Rodents, Vertebrates

REGISTRY NUMBER: 346670-96-0 (NW-1029)

L47 ANSWER 24 OF 34 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STNACCESSION NUMBER: 2002:3675 BIOSIS Full-text

DOCUMENT NUMBER: PREV200200003675

TITLE: Characterization of MAO-B inhibitory properties of
Safinamide (NW-1015) in animals and healthy volunteers.AUTHOR(S): Caccia, C. P. [Reprint author]; Musanti, R. [Reprint
author]; Calabresi, M. [Reprint author]; Lamberti, E.
[Reprint author]; Tocchetti, P.; Dal Bo, L.; Fariello, R.
G. [Reprint author]; Benatti, L. [Reprint author];
Salvati, F. [Reprint author]

CORPORATE SOURCE: Newron Pharmaceuticals, CNS, Gerenzano, Italy

SOURCE: Society for Neuroscience Abstracts, (2001) Vol. 27, No. 2,
pp. 2294. print.Meeting Info.: 31st Annual Meeting of the Society for
Neuroscience. San Diego, California, USA. November 10-15,
2001.

ISSN: 0190-5295.

DOCUMENT TYPE: Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 28 Dec 2001

Last Updated on STN: 26 Feb 2002

ABSTRACT: Safinamide is a novel compound under development for Parkinson's Disease (PD). Aim of the present study is to characterize its MAO-B inhibitory properties in animal models and healthy volunteers. Safinamide potently and reversibly inhibited *in vitro* human platelet MAO-B ($IC_{50}=9$ nM). Selectivity of MAO-B vs MAO-A was about 5000 fold in rat brain. In *ex vivo* studies in mice, MAO-B inhibition peaked at 1h, with complete reversal at 24h. The ED₅₀ was 0.6 mg/kg; ip, with no effects on MAO-A. Safinamide (10-20 mg/kg; ip) did not modify the pressor response to tyramine in conscious rats. In healthy volunteers (n=13) single oral doses (25-600 mug/kg) caused significant, progressive inhibition of platelet MAO-B activity ($ED_{50}=87.5$ mug/kg). At this dosage plasma levels of Safinamide were in the range of 25 pmoles/ml. No effect on MAO-A was reported up to 10 mg/kg; po. When Safinamide was orally administered for 13 weeks (10 and 20 mg/kg) to monkeys, a significant elevation of DA in the putamen (+27% and +48% respectively) and a concomitant decrease of DOPAC were seen at 24h after last intake, indicating increased availability of DA at the synaptic level. These effects occurred with Safinamide plasma concentrations of 241 and 596 pmoles/ml respectively; the same concentrations were reached after single oral doses of 300 and 600 mug/kg in humans.

CONCLUSIONS: Safinamide is a potent and selective MAO-B inhibitor in both animals and humans. Data in primates suggest that Safinamide plasma levels reached at clinical doses will be reflected in enhanced neostriatal DAergic function and symptomatic relief of PD symptoms.

CONCEPT CODE: General biology - Symposia, transactions and proceedings
00520Biochemistry studies - Proteins, peptides and amino acids
10064

Pathology - Therapy 12512

Blood - Blood and lymph studies 15002

Blood - Blood cell studies 15004

Nervous system - Physiology and biochemistry 20504

10/586494

INDEX TERMS:
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Major Concepts
 Nervous System (Neural Coordination); Pharmacology
INDEX TERMS:
Parts, Structures, & Systems of Organisms
 brain: nervous system; plasma: blood and lymphatics;
 platelet: blood and lymphatics; putamen: nervous system;
 synapse: nervous system
INDEX TERMS:
Chemicals & Biochemicals
 DOPAC: regulation; MAO-A [monoamine oxidase-A]; MAO-B
 [monoamine oxidase-B]; dopamine: regulation; safinamide
 [NW-1015]: monoamine oxidase inhibitor-drug, dosage,
 intraperitoneal administration, oral administration,
 plasma; tyramine
INDEX TERMS:
Miscellaneous Descriptors
 Meeting Abstract
ORGANISM:
Classifier
 Hominidae 86215
Super Taxa
 Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
 human
Taxa Notes
 Animals, Chordates, Humans, Mammals, Primates,
 Vertebrates
ORGANISM:
Classifier
 Primates 86190
Super Taxa
 Mammalia; Vertebrata; Chordata; Animalia
Organism Name
 monkey: animal model
Taxa Notes
 Animals, Chordates, Mammals, Nonhuman Mammals, Nonhuman
 Vertebrates, Nonhuman Primates, Primates, Vertebrates
REGISTRY NUMBER:
102-32-9 (DOPAC)
72-44-6 (MAO-A)
72-44-6 (monoamine oxidase-A)
51-61-6 (dopamine)
133865-89-1 (safinamide)
133865-89-1 (NW-1015)
51-67-2 (tyramine)
202825-46-5 (NW-1015)

L47 ANSWER 25 OF 34 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN
ACCESSION NUMBER: 2001:575463 BIOSIS Full-text
DOCUMENT NUMBER: PREV200100575463
TITLE: 2-Methylpropanamides with Na⁺ blocking activity are
effective in electrical and chemical models of seizures.
AUTHOR(S): Maj, R. [Reprint author]; Salvati, P. [Reprint author];
Faravelli, L. [Reprint author]; Musanti, S. [Reprint
author]; Bonsignori, A. [Reprint author]; Veneroni, O.
[Reprint author]; Caccia, C. [Reprint author]; Benatti,
L. [Reprint author]; Fariello, R. G. [Reprint author]
CORPORATE SOURCE: CNS, Newron Pharmaceuticals, Gerenzano, Italy
SOURCE: Society for Neuroscience Abstracts, (2001) Vol. 27, No. 2,
pp. 2004. print.
Meeting Info.: 31st Annual Meeting of the Society for
Neuroscience. San Diego, California, USA. November 10-15,
2001.

DOCUMENT TYPE: Conference; (Meeting)
 Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 12 Dec 2001
 Last Updated on STN: 25 Feb 2002

ABSTRACT: We report on the Na⁺ blocking effects in vitro and anticonvulsant activity and safety in vivo of compounds belonging to the chemical class of 2-methylpropanamides. All compounds displayed affinity for the Na⁺ channel binding site II in the 1-5 μM range, in rat brain membranes. This effect was paralleled by a voltage and use-dependent blockade of Na⁺ currents in neuronal cell cultures and in vivo activity in models of electrically (MES) and chemically-induced seizures in mice. Anticonvulsant potency (ED50) in the MES was between 2.0 and 10.0 mg/kg after both po and ip administration. In chemical seizures, such as systemic injection of pentylenetetrazol and bicuculline, ED50 was between 6 and 18 mg/kg; ip. Moreover several molecules displayed a good oral therapeutic index (ratio between ED50 and rotarod TD50) ranging from 25 to 100, that compares very favourable with the antiepileptic drugs used in clinical practice. NW-1063 emerged as one of the most interesting compounds among this class, for its good anticonvulsant activity and high safety margin. To better characterize its anticonvulsant profile, NW-1063 was also tested in the amygdala kindling model of complex partial seizures in rats. Seizure duration was significantly shortened starting from the dose of 1 mg/kg; ip. These results demonstrate that this class of Na⁺ channel blockers display good anticonvulsant activity with a rather wide safety margin. NW-1063 anticonvulsant spectrum of efficacy is under broader and deeper investigation in a battery of seizure and epilepsy models.

CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520
 Cytology - Animal 02506
 Biochemistry studies - General 10060
 Biochemistry studies - Minerals 10069
 Enzymes - General and comparative studies: coenzymes 10802
 Pathology - Therapy 12512
 Nervous system - Physiology and biochemistry 20504
 Nervous system - Pathology 20506
 Pharmacology - General 22002
 Pharmacology - Neuropharmacology 22024

INDEX TERMS: Major Concepts
 Nervous System (Neural Coordination); Pharmacology

INDEX TERMS: Parts, Structures, & Systems of Organisms
 amygdala: nervous system; brain membrane: nervous system; neuronal cell: nervous system

INDEX TERMS: Diseases
 complex partial seizure: nervous system disease, duration, treatment
 Seizures (MeSH)

INDEX TERMS: Diseases
 seizures: nervous system disease, duration, treatment
 Seizures (MeSH)

INDEX TERMS: Chemicals & Biochemicals
 2-methylpropanamide: anticonvulsant, efficacy, pharmacodynamics, sodium channel blocker; NW-1603: anticonvulsant-drug, efficacy, intraperitoneal administration, oral administration, pharmacodynamics, safety; bicuculline; pentylenetetrazol [pentylenetetrazole]; sodium; sodium ion channel; sodium ion channel binding site II

INDEX TERMS: Methods & Equipment

INDEX TERMS: oral therapeutic index: assessment method
 Miscellaneous Descriptors
 sodium ion current; Meeting Abstract
 ORGANISM: Classifier
 Muridae 86375
 Super Taxa
 Rodentia; Mammalia; Vertebrata; Chordata; Animalia
 Organism Name
 mouse: animal model
 rat
 Taxa Notes
 Animals, Chordates, Mammals, Nonhuman Vertebrates,
 Nonhuman Mammals, Rodents, Vertebrates
 REGISTRY NUMBER: 563-83-7 (2-methylpropanamide)
 485-49-4 (bicuculline)
 54-95-5 (pentylenetetrazol)
 54-95-5 (pentylenetetrazole)
 7440-23-5 (sodium)

L47 ANSWER 26 OF 34 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
 STN

ACCESSION NUMBER: 2001:109692 BIOSIS Full-text
 DOCUMENT NUMBER: PREV200100109692
 TITLE: NW-1048 is a novel, reversible and selective MAO-B inhibitor with neuroprotective effects in a model of Parkinson's disease.
 AUTHOR(S): Salvati, P. [Reprint author]; Caccia, C.; Maj, R.; Musanti, R.; Lamberti, E.; Calabresi, M.; Benatti, L.; Fariello, R. G.
 CORPORATE SOURCE: Newron Pharmaceuticals, Gerenzano VA, Italy
 SOURCE: Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-765.11. print.
 Meeting Info.: 30th Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 04-09, 2000.
 Society for Neuroscience.
 ISSN: 0190-5295.
 DOCUMENT TYPE: Conference; (Meeting)
 Conference; Abstract; (Meeting Abstract)
 LANGUAGE: English
 ENTRY DATE: Entered STN: 28 Feb 2001
 Last Updated on STN: 15 Feb 2002

ABSTRACT:MAO-B inhibitors possess the ability to improve motor function in Parkinson's Disease (PD) by decreasing dopamine (DA) metabolism, when used associated to L-dopa. Recently it has been suggested that they might also slow down disease progression possibly by reducing oxidative damage. NW-1048 selectively and reversibly inhibits human platelet MAO-B ($IC_{50}=30nM$) ; and also inhibits rat brain MAO-B with more than 400 times higher selectivity for MAO-B relative to MAO-A. Ex vivo brain MAO-B activity was still significantly inhibited 8 h (48%), after ip administration of 20 mg/kg to mice. The neuroprotective effect of NW-1048 on nigrostriatal DA neurons was studied in MPTP (40 mg/kg; sc x 2) treated C57-BL mice. At 15 days after injection, MPTP induced a significant decrease of striatal DA levels (89%) and striatal and nigral tyrosine hydroxylase (TH) activity (84 and 60% respectively). NW-1048 (10 mg/kg; ip 30 min before MPTP injection) completely prevented these effects. Significant protection of striatal TH activity was found even when the compound was administered 4 h after MPTP. Furthermore in the same model, co-administration of NW-1048 (10 and 20 mg/kg; ip) and L-dopa (100 mg/kg; ip) + benserazide (12.5 mg/kg; ip) resulted in significantly higher DA striatal levels than after L-dopa + benserazide alone. CONCLUSIONS: Results indicate that NW-1048 has neuroprotective and neurorescuing effects in the mouse MPTP

10/586494

model and potentiates L-dopa-mediated increase in DA levels. NW-1048 might therefore be used in PD to reduce L-dopa dosage and also might represent a valuable therapeutic treatment to slow down disease progression.

CONCEPT CODE: Nervous system - Pathology 20506
General biology - Symposia, transactions and proceedings 00520
Biochemistry studies - Proteins, peptides and amino acids 10064
Enzymes - General and comparative studies: coenzymes 10802
Nervous system - Physiology and biochemistry 20504

INDEX TERMS: Major Concepts
Nervous System (Neural Coordination)

INDEX TERMS: Parts, Structures, & Systems of Organisms
brain: nervous system; striatum: nervous system

INDEX TERMS: Diseases
Parkinson's disease: nervous system disease
Parkinson Disease (MeSH)

INDEX TERMS: Chemicals & Biochemicals
L-dopa; MAO-B inhibitor; MPTP; NW-1048: MAO-B inhibitor, neuroprotective effects, neurorescuing effects; benserazide; dopamine; tyrosine hydroxylase

INDEX TERMS: Miscellaneous Descriptors
Meeting Abstract

ORGANISM: Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
mouse: strain-C57-BL
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

REGISTRY NUMBER: 28289-54-5 (MPTP)
322-35-0 (benserazide)
51-61-6 (dopamine)
9036-22-0 (tyrosine hydroxylase)

L47 ANSWER 27 OF 34 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:88995 BIOSIS Full-text
DOCUMENT NUMBER: PREV200100088995
TITLE: NW-1029 is a novel Na⁺ channel blocker, with analgesic activity in animal models.
AUTHOR(S): Faravelli, L. [Reprint author]; Maj, R.; Veneroni, O.; Fariello, R. G.; Benatti, L.; Salvati, P.
CORPORATE SOURCE: Newron Pharmaceuticals, Gerenzano, Italy
SOURCE: Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-454.9. print.
Meeting Info.: 30th Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 04-09, 2000.
Society for Neuroscience.
ISSN: 0190-5295.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Feb 2001
Last Updated on STN: 12 Feb 2002
ABSTRACT: Small diameter, nociceptive sensory neurons of the dorsal root ganglion (DRG) express both the rapidly inactivating TTX sensitive (TTXS) and

the more slowly inactivating TTX resistant (TTXR) Na⁺ current. Recent experimental evidence pointed out Na⁺ currents as important targets to studying the molecular pathophysiology of pain and to searching new pain therapies. NW-1029 is a novel Na⁺ channel blocker, showing selective affinity for the 3H-batrachotoxin binding sites (IC₅₀ = 1.4 μM) in rat brain membranes. Aim of the present study was to evaluate its inhibitory activity on TTXS and TTXR Na⁺ currents in DRG neurons by means of the whole cell patch clamp technique and to test its analgesic activity in animal models of pain. NW-1029 caused a concentration dependent inhibition of both TTXR and TTXS Na⁺ currents. The functional importance of the use-dependent block of these currents was confirmed in current clamped DRG neurons, where NW-1029 modulated firing activity. The potential analgesic activity of NW-1029 was examined in the mice formalin model of persistent pain and in the chronic constriction injury (CCI) model of neuropathic pain. NW-1029 dose dependently reduced cumulative licking time in the late phase of the formalin test (from 123 to 66 sec, P < 0.01 at 10 mg/kg; po), and significantly increased mechanical allodynia threshold (Von Frey test) in the CCI rat model (from 0.22 to 10 g, at the dose of 3 mg/kg; ip, 2 h after treatment). CONCLUSIONS: The results of this study indicate that the inhibitory effects of NW-1029 on Na⁺ currents expressed in DRG sensory neurons might provide the basis for its marked antihyperalgesic action in animal models.

CONCEPT CODE:

- Nervous system - Pathology 20506
- General biology - Symposia, transactions and proceedings 00520
- Cytology - Animal 02506
- Biochemistry studies - General 10060
- Nervous system - Physiology and biochemistry 20504

INDEX TERMS:

- Major Concepts
 - Biochemistry and Molecular Biophysics; Nervous System (Neural Coordination)

INDEX TERMS:

- Parts, Structures, & Systems of Organisms
 - brain membranes: nervous system; dorsal root ganglion: nervous system; sensory neurons: nervous system, nociceptive

INDEX TERMS:

- Diseases
 - chronic constriction injury: injury

INDEX TERMS:

- Diseases
 - neuropathic pain: nervous system disease
 - Pain (MeSH)

INDEX TERMS:

- Chemicals & Biochemicals
 - NW-1029: sodium positive ion channel blocker; [tritiated] batrachotoxin: binding sites; sodium positive ion currents

INDEX TERMS:

- Methods & Equipment
 - Von Frey test: assessment method

INDEX TERMS:

- Miscellaneous Descriptors
 - Meeting Abstract

ORGANISM:

- Classifier
 - Muridae 86375
- Super Taxa
 - Rodentia; Mammalia; Vertebrata; Chordata; Animalia
- Organism Name
 - rat
- Taxa Notes
 - Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

REGISTRY NUMBER: 346670-96-0 (NW-1029)

10/586494

ACCESSION NUMBER: 2000:147663 BIOSIS Full-text
DOCUMENT NUMBER: PREV200000147663
TITLE: PNU-151774E, a novel NA⁺ channel blocker, shows analgesic effects in some animal models.
AUTHOR(S): Salvati, P. [Reprint author]; Maj, R. [Reprint author]; Mc Arthur, R. A.; Cervini, M. A.; Kozak, W.; Benatti, L. [Reprint author]; Fariello, R. G. [Reprint author]
CORPORATE SOURCE: Newron Pharmaceuticals, Gerenzano (VA), I-21040, Italy
SOURCE: Society for Neuroscience Abstracts, (1999) Vol. 25, No. 1-2, pp. 1947. print.
Meeting Info.: 29th Annual Meeting of the Society for Neuroscience. Miami Beach, Florida, USA. October 23-28, 1999. Society for Neuroscience.
ISSN: 0190-5295.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 19 Apr 2000
Last Updated on STN: 4 Jan 2002
CONCEPT CODE: Nervous system - General and methods 20501
Biochemistry studies - General 10060
Biophysics - General 10502
Pharmacology - General 22002
General biology - Symposia, transactions and proceedings 00520
INDEX TERMS: Major Concepts
 Nervous System (Neural Coordination); Pharmacology
INDEX TERMS: Diseases
 chronic pain: nervous system disease
 Pain (MeSH)
INDEX TERMS: Diseases
 neuropathic pain: nervous system disease
 Pain (MeSH)
INDEX TERMS: Chemicals & Biochemicals
 PNU-151774E: analgesic-drug, sodium ion channel blocker
INDEX TERMS: Miscellaneous Descriptors
 allodynia; hyperalgesia; locomotor activity; spontaneous pain; Meeting Abstract
ORGANISM: Classifier
 Animalia 33000
Super Taxa
 Animalia
Organism Name
 animal: animal model
Taxa Notes
 Animals
Classifier
 Muridae 86375
Super Taxa
 Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
 mouse: animal model
Taxa Notes
 Animals, Chordates, Mammals, Nonhuman Vertebrates,
 Nonhuman Mammals, Rodents, Vertebrates
REGISTRY NUMBER: 202825-46-5 (PNU-151774E)

L47 ANSWER 29 OF 34 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN

ACCESSION NUMBER: 1997:533505 BIOSIS Full-text

10/586494

DOCUMENT NUMBER: PREV199799832708
TITLE: Induction of ZFM1 mRNA, encoding a novel nuclear protein, in rat brain after global ischemia.
AUTHOR(S): Covini, N.; Consalez, G. [Reprint author]; Salvati, P.; Benatti, L.
CORPORATE SOURCE: DIBIT Res. Cent., HSR, Milan, Italy
SOURCE: Society for Neuroscience Abstracts, (1997) Vol. 23, No. 1-2, pp. 2181.
Meeting Info.: 27th Annual Meeting of the Society for Neuroscience. New Orleans, Louisiana, USA. October 25-30, 1997.
ISSN: 0190-5295.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Dec 1997
Last Updated on STN: 12 Dec 1997
CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520
Biochemistry studies - General 10060
Cardiovascular system - General and methods 14501
Nervous system - General and methods 20501
INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Cardiovascular System (Transport and Circulation); Nervous System (Neural Coordination)
INDEX TERMS: Miscellaneous Descriptors
CARDIOVASCULAR SYSTEM; CEREBRAL ISCHEMIA; HUMAN ZINC FINGER MOTIF-1 HOMOLOG; MESSENGER RNA INDUCTION; NERVOUS SYSTEM; NERVOUS SYSTEM DISEASE; PH3.3; P53; VASCULAR DISEASE; ZINC FINGER MOTIF-1
ORGANISM: Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
rat
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

L47 ANSWER 30 OF 34 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 1996:547841 BIOSIS Full-text
DOCUMENT NUMBER: PREV199699270197
TITLE: Temporal and spatial changes of quinolinic acid immunoreactivity in the hippocampus following transient forebrain ischemia.
AUTHOR(S): Baratte, S.; Molinari, A.; Veneroni, O.; Dho, L.; Speciale, C.; Benatti, L.; Salvati, P.
CORPORATE SOURCE: Pharamcia and Upjohn, CNS Res., Nerviano, Italy
SOURCE: Society for Neuroscience Abstracts, (1996) Vol. 22, No. 1-3, pp. 1795.
Meeting Info.: 26th Annual Meeting of the Society for Neuroscience. Washington, D.C., USA. November 16-21, 1996.
ISSN: 0190-5295.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)

10/586494

LANGUAGE: English
ENTRY DATE: Entered STN: 13 Dec 1996
Last Updated on STN: 13 Dec 1996
CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520
Cytology - Animal 02506
Movement 12100
Pathology - Inflammation and inflammatory disease 12508
Cardiovascular system - Blood vessel pathology 14508
Blood - Lymphatic tissue and reticuloendothelial system 15008
Nervous system - Pathology 20506
Immunology - Immunopathology, tissue immunology 34508
INDEX TERMS: Major Concepts
Blood and Lymphatics (Transport and Circulation);
Cardiovascular System (Transport and Circulation); Cell Biology; Immune System (Chemical Coordination and Homeostasis); Nervous System (Neural Coordination); Pathology
INDEX TERMS: Chemicals & Biochemicals
QUINOLINIC ACID; L-TRYPTOPHAN
INDEX TERMS: Miscellaneous Descriptors
HIPPOCAMPUS; IMMUNE SYSTEM; IMMUNOREACTIVITY;
INFLAMMATION; L-TRYPTOPHAN METABOLITES; MEETING ABSTRACT; MEETING POSTER; MICROGLIAL-LIKE CELL INFILTRATION; NERVOUS SYSTEM; NERVOUS SYSTEM DISEASE; NEURODEGENERATION; QUINOLINIC ACID; TRANSIENT FOREBRAIN ISCHEMIA; VASCULAR DISEASE
ORGANISM: Classifier
Cricetidae 86310
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
gerbil
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates,
Nonhuman Mammals, Rodents, Vertebrates
ORGANISM: Classifier
Leporidae 86040
Super Taxa
Lagomorpha; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
rabbit
Taxa Notes
Animals, Chordates, Lagomorphs, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Vertebrates
REGISTRY NUMBER: 89-00-9 (QUINOLINIC ACID)
73-22-3 (L-TRYPTOPHAN)

L47 ANSWER 31 OF 34 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN
ACCESSION NUMBER: 1996:553477 BIOSIS Full-text
DOCUMENT NUMBER: PREV199699275833
TITLE: FCE 28833A, a potent inhibitor of kynureneine 3-hydroxylase, enhances brain kynurenic acid and is neuroprotective in the gerbil ischemia model.
AUTHOR(S): Speciale, C. [Reprint author]; Salvati, P. [Reprint author]; Cini, M. [Reprint author]; Benatti, L. [Reprint author]; Tamburin, M. [Reprint author]; Molinari, A. [Reprint author]; Rosa, B. [Reprint author]; Allievi, C.;

10/586494

CACCIA, C. [Reprint author]; VARASI, M. [Reprint author];
POST, C. [Reprint author]
CORPORATE SOURCE: Pharmacia Upjohn, CNS Res., Nerviano, Italy
SOURCE: Society for Neuroscience Abstracts, (1996) Vol. 22, No.
1-3, pp. 1542.
Meeting Info.: 26th Annual Meeting of the Society for
Neuroscience. Washington, D.C., USA. November 16-21, 1996.
ISSN: 0190-5295.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Dec 1996
Last Updated on STN: 13 Dec 1996
CONCEPT CODE: General biology - Symposia, transactions and proceedings
00520
Cytology - Animal 02506
Biochemistry studies - Proteins, peptides and amino acids
10064
Enzymes - Physiological studies 10808
Cardiovascular system - Blood vessel pathology 14508
Nervous system - Pathology 20506
Pharmacology - Neuropharmacology 22024
INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Cardiovascular
System (Transport and Circulation); Cell Biology;
Enzymology (Biochemistry and Molecular Biophysics);
Nervous System (Neural Coordination); Pharmacology
INDEX TERMS: Chemicals & Biochemicals
KYNURENINE 3-HYDROXYLASE; KYNURENIC ACID
INDEX TERMS: Miscellaneous Descriptors
(R,S)-3,4-DICHLOROBENZOYLALANINE; ANIMAL MODEL; FCE
28833A; ISCHEMIA; KYNURENIC ACID; KYNURENINE
3-HYDROXYLASE INHIBITOR; MEETING ABSTRACT; MEETING
POSTER; NERVOUS SYSTEM; NEURONAL LOSS; NEUROPROTECTION;
PHARMACOLOGY; VASCULAR DISEASE
ORGANISM: Classifier
Cricetidae 86310
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
gerbil
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates,
Nonhuman Mammals, Rodents, Vertebrates
REGISTRY NUMBER: 9029-61-2 (KYNURENINE 3-HYDROXYLASE)
492-27-3 (KYNURENIC ACID)

L47 ANSWER 32 OF 34 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN
ACCESSION NUMBER: 1993:539967 BIOSIS Full-text
DOCUMENT NUMBER: PREV199345127061
TITLE: Renal endothelin (ET-1) and ET-beta receptor gene
expression in NZB/W F-1 mice with lupus nephritis.
AUTHOR(S): Benatti, L. [Reprint author]; Tamburin, M.; Bonecchi, L.;
Lamberti, E.; Ferrario, R. G.; Salvati, P.; Patrono, C.
CORPORATE SOURCE: Farmitalia Carlo Erba-Biotechnol., Nerviano, Italy
SOURCE: Journal of the American Society of Nephrology, (1993) Vol.
4, No. 3, pp. 764.
Meeting Info.: 26th Annual Meeting of the ASN (American

Society of Nephrology). Boston, Massachusetts, USA.
 November 14-17, 1993.
 CODEN: JASNEU. ISSN: 1046-6673.

DOCUMENT TYPE: Conference; (Meeting)
 LANGUAGE: English
 ENTRY DATE: Entered STN: 30 Nov 1993
 Last Updated on STN: 30 Nov 1993
 CONCEPT CODE: General biology - Symposia, transactions and proceedings
 00520
 Genetics - Animal 03506
 Biochemistry studies - Proteins, peptides and amino acids
 10064
 Pathology - Inflammation and inflammatory disease 12508
 Metabolism - Proteins, peptides and amino acids 13012
 Urinary system - Pathology 15506
 Endocrine - Neuroendocrinology 17020
 Integumentary system - Pathology 18506
 Nervous system - Physiology and biochemistry 20504
 Immunology - Immunopathology, tissue immunology 34508

INDEX TERMS: Major Concepts
 Endocrine System (Chemical Coordination and Homeostasis); Genetics; Immune System (Chemical Coordination and Homeostasis); Integumentary System (Chemical Coordination and Homeostasis); Metabolism; Nervous System (Neural Coordination); Pathology; Urinary System (Chemical Coordination and Homeostasis)

INDEX TERMS: Chemicals & Biochemicals
 ET-1

INDEX TERMS: Miscellaneous Descriptors
 ABSTRACT; CHRONIC RENAL FAILURE; PATHOPHYSIOLOGY

ORGANISM: Classifier
 Muridae 86375
 Super Taxa
 Rodentia; Mammalia; Vertebrata; Chordata; Animalia
 Organism Name
 Muridae
 Taxa Notes
 Animals, Chordates, Mammals, Nonhuman Vertebrates,
 Nonhuman Mammals, Rodents, Vertebrates

REGISTRY NUMBER: 76543-79-8 (ET-1)

L47 ANSWER 33 OF 34 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
 ACCESSION NUMBER: 2008-F09832 [35] WPIX Full-text
 CROSS REFERENCE: 2005-736600
 DOC. NO. CPI: C2008-167962 [35]
 TITLE: Use of e.g. 2-(4-benzyloxybenzylamino)propanamide,
 2-(4-(2-methoxybenzyloxy)-benzylamino)propanamide and
 2-(4-(2-fluorobenzyloxy)-benzylamino)propanamide, for
 treating addictive disorders and restless leg syndrome
 B05
 DERWENT CLASS:
 INVENTOR: BARBANTI E; BENATTI L; BESANA C; FARIELLO R; IZZO E;
 SALVATI P; THALER F
 PATENT ASSIGNEE: (NEWR-N) NEWRON PHARM SPA
 COUNTRY COUNT: 33

PATENT INFORMATION:

PATENT NO	KIND DATE	WEEK	LA	PG	MAIN IPC
EP 1900362	A2 20080319 (200835)*	EN	12[0]		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 1900362 A2	Div Ex	EP 2005-736365	20050419
EP 1900362 A2		EP 2007-22078	20050419

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1900362	A2	Div ex
		EP 1737438 A

PRIORITY APPLN. INFO: EP 2004-9532 20040422

INT. PATENT CLASSIF.:

IPC ORIGINAL: A61K0031-165 [I,A]; A61K0031-165 [I,C]; A61K0031-185 [I,C]; A61K0031-198 [I,A]; A61K0031-381 [I,A]; A61K0031-381 [I,C]; A61K0031-40 [I,A]; A61K0031-40 [I,C]; A61K0045-00 [I,C]; A61K0045-06 [I,A]; A61P0025-00 [I,C]; A61P0025-14 [I,A]; A61P0025-30 [I,A]; A61P0025-32 [I,A]; A61P0025-34 [I,A]; A61P0025-36 [I,A]

ECLA: A61K0031-165; A61K0031-165+M; A61K0031-198; A61K0031-198+M; A61K0031-381; A61K0031-381+M; A61K0031-40; A61K0031-40+M; A61K0045-06

BASIC ABSTRACT:

EP 1900362 A2 UPAB: 20080604

NOVELTY - Use of 51 aminoamide compounds (A) e.g. 2-(4-benzyloxybenzylamino)propanamide, 2-(4-(2-methoxybenzyloxy)-benzylamino)propanamide, 2-(4-(2-fluorobenzyloxy)-benzylamino)propanamide, (S)-(+)2-(4-(2-fluorobenzyloxy)-benzylamino)propanamide, 2-(4-(2-fluorobenzyloxy)-benzylamino)-2-methyl-propanamide, 2-(4-(2-fluorobenzyloxy)-benzylamino)-N-methyl-propanamide and N-(2-(4-(2-fluorobenzyloxy)-benzylamino))pro-pionyl-pyrrolidine compounds and their isomers, mixtures, or salts, for the preparation of a medicament to treat addictive disorders, is claimed.

DETAILED DESCRIPTION - Use of aminoamide compounds (A) comprising e.g. 2-(4-benzyloxybenzylamino)propanamide, 2-(4-(2-methoxybenzyloxy)-benzylamino)propanamide, 2-(4-(2-fluorobenzyloxy)-benzylamino)propanamide, (S)-(+)2-(4-(2-fluorobenzyloxy)-benzylamino)propanamide, 2-(4-(2-fluorobenzyloxy)-benzylamino)-2-methyl-propanamide, 2-(4-(2-fluorobenzyloxy)-benzylamino)-N-methyl-propanamide, N-(2-(4-(2-fluorobenzyloxy)-benzylamino))pro-pionyl-pyrrolidine, 2-(4-(3-methoxybenzyloxy)-benzylamino)propanamide, 2-(4-(3-chlorobenzyloxy)-benzylamino)propanamide, 2-(4-benzyloxybenzylamino)-3-hydroxy-propanamide, 2-(4-(3-chlorobenzyloxy)-phenylethylamino)propanamide, 2-(4-benzyloxybenzylamino)-2-phenyl-acetamide, 2-(4-(2-fluorobenzyloxy)-benzylamino)-2-(3-fluorophenyl)-acetamide, and their isomers, mixtures, or salts, for the preparation of a medicament for treating addictive disorders, is claimed.

ACTIVITY - Muscular-Gen.; Antiaddictive.

MECHANISM OF ACTION - Monoamine oxidase B inhibitor; Sodium channel blocker; Dopamine reuptake inhibitor; Glutamate level modulator.

USE - (A) is useful to treat an addictive disorder (claimed) and restless leg syndrome. The ability of (I) to treat drug abuse was tested in rats using a discrimination assay. The result showed that (I) exhibited the ED50 value of greater than 80%.

ADVANTAGE - (A) reduces the symptoms of restless leg syndrome and addictive disorders without side effects. MANUAL CODE: CPI: B07-B01; B10-A15; B10-A19; B10-B02E; B10-D03; B14-D05A; B14-J05A; B14-L01; B14-L06; B14-M01C

L47 ANSWER 34 OF 34 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
 ACCESSION NUMBER: 2005-556814 [57] WPIX Full-text
 DOC. NO. CPI: C2007-041238 [12]
 TITLE: Use of alpha-aminoamide compounds having sodium channel blocking activity for preparation of medicament to treat lower urinary tract disorders e.g. overactive bladder, prostatitis, prostdynia and benign prostatic hyperplasia
 B02; B03
 DERWENT CLASS:
 INVENTOR: BARBANTI E; BENATTI L; PELLICCIARI R; SALVATI P;
 THALER F; VENERONI O; SAALVATI P
 PATENT ASSIGNEE: (NEWRON PHARM SPA; (BARB-I) BARBANTI E; (BENA-I)
 BENATTI L; (PELL-I) PELLICCIARI R; (SALV-I) SALVATI P;
 (THAL-I) THALER F; (VENE-I) VENERONI O
 COUNTRY COUNT: 107

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
EP 1557166	A1	20050727	(200557)*	EN	21[3]	
WO 2005070405	A1	20050804	(200557)	EN		
NO 2006003368	A	20061012	(200675)	NO		
AU 2005205903	A1	20050804	(200707)	EN		
MX 2006008188	A1	20061101	(200737)	ES		
BR 2005006970	A	20070703	(200746)	PT		
JP 2007518763	W	20070712	(200746)	JA	29	
KR 2007007776	A	20070116	(200755)	KO		
CN 1956714	A	20070502	(200760)	ZH		
IN 2006DN04152	P1	20070810	(200780)	EN		
US 20080132567	A1	20080605	(200838)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 1557166 A1		EP 2004-1175	20040121
AU 2005205903 A1		AU 2005-205903	20050120
BR 2005006970 A		BR 2005-6970	20050120
CN 1956714 A		CN 2005-80002785	20050120
WO 2005070405 A1		WO 2005-EP514	20050120
NO 2006003368 A		WO 2005-EP514	20050120
MX 2006008188 A1		WO 2005-EP514	20050120
BR 2005006970 A		WO 2005-EP514	20050120
JP 2007518763 W		WO 2005-EP514	20050120
KR 2007007776 A		WO 2005-EP514	20050120
IN 2006DN04152 P1		WO 2005-EP514	20050120
JP 2007518763 W		JP 2006-550030	20050120
IN 2006DN04152 P1		IN 2006-DN4152	20060719
MX 2006008188 A1		MX 2006-8188	20060719
KR 2007007776 A		KR 2006-714655	20060720
NO 2006003368 A		NO 2006-3368	20060720
US 20080132567 A1		WO 2005-EP514	20050120
US 20080132567 A1		US 2007-586494	20070125

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2005205903	A1	Based on WO 2005070405 A

MX 2006008188	A1	Based on	WO 2005070405	A
BR 2005006970	A	Based on	WO 2005070405	A
JP 2007518763	W	Based on	WO 2005070405	A
KR 2007007776	A	Based on	WO 2005070405	A

PRIORITY APPLN. INFO: EP 2004-1175 20040121

INT. PATENT CLASSIF.:

MAIN: A61K031-165

IPC ORIGINAL: A61K0031-135 [I,A]; A61K0031-165 [I,A]; A61K0031-165 [I,A]; A61K0031-165 [I,C]; A61K0031-165 [I,C]; A61K0031-165 [I,C]; A61K0031-275 [I,C]; A61K0031-277 [I,A]; A61K0031-277 [I,A]; A61K0031-34 [I,A]; A61K0031-34 [I,A]; A61K0031-34 [I,A]; A61K0031-34 [I,C]; A61K0031-343 [I,A]; A61K0031-343 [I,A]; ; A61K0031-343 [I,C]; A61K0031-343 [I,C]; A61K0031-352 [I,C]; A61K0031-353 [I,A]; A61K0031-353 [I,A]; A61K0031-381 [I,A]; A61K0031-381 [I,A]; A61K0031-381 [I,C]; A61K0031-4015 [I,A]; A61K0031-4015 [I,A]; A61K0031-4015 [I,A]; A61K0031-4015 [I,C]; A61K0031-551 [I,A]; A61K0031-551 [I,C]; A61P0013-00 [I,C]; A61P0013-00 [I,C]; A61P0013-02 [I,A]; A61P0013-02 [I,A]; A61P0013-08 [I,A]; A61P0013-08 [I,A]; A61P0013-10 [I,A]; A61P0013-10 [I,A]; A61P0025-00 [I,C]; A61P0025-04 [I,A]; C07D0307-00 [I,C]; C07D0307-00 [I,C]; C07D0307-00 [I,C]; C07D0307-00 [I,C]; C07D0307-77 [I,A]; C07D0307-79 [I,A]; C07D0307-79 [I,A]; C07D0307-79 [I,A]; C07D0311-00 [I,C]; C07D0311-20 [I,A]; C07D0311-20 [I,A]; C07D0313-04 [I,A]; C07D0321-00 [N,C]; C07D0321-10 [N,A]; C07D0333-54 [I,A]

IPC RECLASSIF.: A61K0031-165 [I,A]; A61K0031-165 [I,C]; A61K0031-275 [I,C]; A61K0031-277 [I,A]; A61K0031-34 [I,A]; A61K0031-34 [I,C]; A61K0031-352 [I,C]; A61K0031-353 [I,A]; A61K0031-381 [I,A]; A61K0031-381 [I,C]; A61K0031-4015 [I,A]; A61K0031-4015 [I,C]; C07D0307-00 [I,C]; C07D0307-28 [I,A]; C07D0307-79 [I,A]; C07D0311-00 [I,C]; C07D0311-20 [I,A]; C07D0311-58 [I,A]; C07D0313-00 [I,C]; C07D0313-04 [I,A]; C07D0313-08 [I,A]; C07D0333-00 [I,C]; C07D0333-32 [I,A]; C07D0333-54 [I,A]; C07D0333-58 [I,A]

ECLA: A61K0031-165; A61K0031-277; A61K0031-34; A61K0031-353; A61K0031-381; A61K0031-4015; C07D0307-28; C07D0311-58; C07D0313-08; C07D0333-32; C07D0333-58

ICO: M07D0307:28

USCLASS NCLM: 514/469.000

NCLS: 514/620.000; 549/469.000

BASIC ABSTRACT:

EP 1557166 A1 UPAB: 20070227

NOVELTY - Use of alpha-aminoamide compounds (I) or their isomers, mixtures or salts for the preparation of a medicament to treat lower urinary tract disorders.

DETAILED DESCRIPTION - Use of alpha-aminoamide compounds of formula (I) or their isomers, mixtures or salts for the preparation of a medicament to treat lower urinary tract disorders.

R=furyl, thienyl or pyridyl ring or a phenyl ring (all optionally substituted 1-2 substituents of halo, OH, CN, 1-6C alkyl, 1-6C alkoxy or trifluoromethyl;

R1=H or 1-6C alkyl or 3-7C cycloalkyl; either

R2, R3=H, 1-4C alkyl optionally substituted by OH or phenyl (optionally substituted by 1-2 substituents of 1-6C alkyl, halo, OH, 1-6C alkoxy or trifluoromethyl; or

R₂R₃C=a 3-6C cycloalkyl ring; either
R₄, R₅=H, 1-6C alkyl or 3-7C cycloalkyl; or
R₄R₅N=a 5-7 atom saturated heterocyclic ring;
X=CH₂, O or S; either
Y, Z=H; or
YZ=a 5-7 optionally saturated carbocycle or a heterocycle.

INDEPENDENT CLAIMS are also included for an alpha-aminoamide compound of formula (I); and a composition comprising (I) as an active agent and (I).

ACTIVITY - Uropathic; Antiinflammatory; Cytostatic.

(I) were tested for their ability to treat acute bladder irritation by acetic acid in rats. The results showed that (I) (NW-1029) significantly reversed the acetic acid-induction in the intercontraction intervals in rats.

MECHANISM OF ACTION - Sodium channel blocker.

USE - (I) are useful for the treatment of lower urinary tract disorders (overactive bladder, prostatitis, prostdynia, interstitial cystitis, benign prostatic hyperplasia and urinary incontinence) (claimed).

ADVANTAGE - The present invention provides rapid and highly effective methods for treating a variety of lower urinary tract disorders .

MANUAL CODE: CPI: B06-H; B07-H; B10-A15; B10-B02F; B14-H05; B14-L06;
B14-N07

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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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DICTIONARY FILE UPDATES: 12 NOV 2008 HIGHEST RN 1072189-85-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

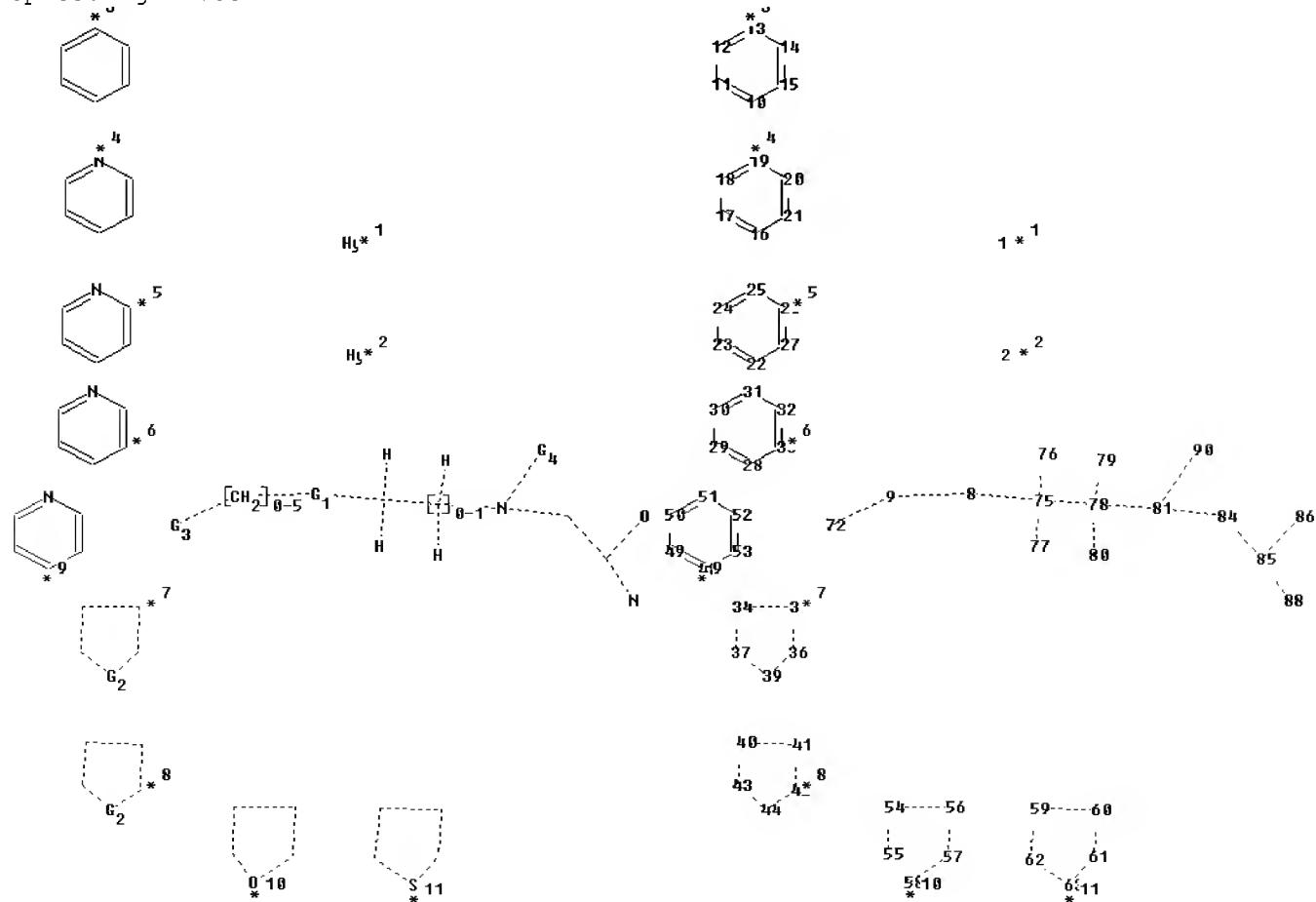
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<http://www.cas.org/support/stngen/stndoc/properties.html>

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chain nodes :
 1 2 8 9 72 75 76 77 78 79 80 81 85 86 90
 ring nodes :
 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30
 31 32 33 34 35 36 37 39 40 41 42 43 44 48 49 50 51 52 53 54 55
 56 57 58
 59 60 61 62 63
 ring/chain nodes :
 84 88
 chain bonds :
 8-9 8-75 9-72 75-76 75-77 75-78 78-79 78-80 78-81 81-84 81-90 84-85 85-
 86
 85-88
 ring bonds :
 10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-21 17-18 18-19 19-20 20-21
 22-23 22-27 23-24 24-25 25-26 26-27 28-29 28-33 29-30 30-31 31-32 32-33
 34-35 34-37
 35-36 36-39 37-39 40-41 40-43 41-42 42-44 43-44 48-49 48-53 49-50 50-51
 51-52 52-53
 54-55 54-56 55-58 56-57 57-58 59-60 59-62 60-61 61-63 62-63
 exact/norm bonds :
 8-9 8-75 9-72 34-35 34-37 35-36 36-39 37-39 40-41 40-43 41-42 42-44 43-
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 54-55 54-56 55-58 56-57 57-58 59-60 59-62 60-61 61-63 62-63 75-76 75-77
 75-78 78-79
 78-80 78-81 81-84 81-90 84-85 85-86 85-88
 normalized bonds :
 10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-21 17-18 18-19 19-20 20-21
 22-23 22-27 23-24 24-25 25-26 26-27 28-29 28-33 29-30 30-31 31-32 32-33
 48-49 48-53
 49-50 50-51 51-52 52-53

G1:[*1], [*2]

G2:O, S

G3:[*3], [*4], [*5], [*6], [*7], [*8], [*9], [*10], [*11]

G4:H, Cb, Ak

Connectivity :
 85:3 E exact RC ring/chain 86:1 E exact RC ring/chain
 Match level :
 1:Atom 2:Atom 8:CLASS 9:CLASS 10:Atom 11:Atom 12:Atom 13:Atom 14:Atom
 15:Atom
 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom 21:Atom 22:Atom 23:Atom 24:Atom
 25:Atom 26:Atom
 27:Atom 28:Atom 29:Atom 30:Atom 31:Atom 32:Atom 33:Atom 34:Atom 35:Atom
 36:Atom 37:Atom
 39:Atom 40:Atom 41:Atom 42:Atom 43:Atom 44:Atom 48:Atom 49:Atom 50:Atom
 51:Atom 52:Atom
 53:Atom 54:Atom 55:Atom 56:Atom 57:Atom 58:Atom 59:Atom 60:Atom 61:Atom
 62:Atom 63:Atom
 72:CLASS 75:CLASS 76:CLASS 77:CLASS 78:CLASS 79:CLASS 80:CLASS 81:CLASS
 84:CLASS 85:CLASS
 86:CLASS 88:CLASS 90:CLASS
 Generic attributes :

10/586494

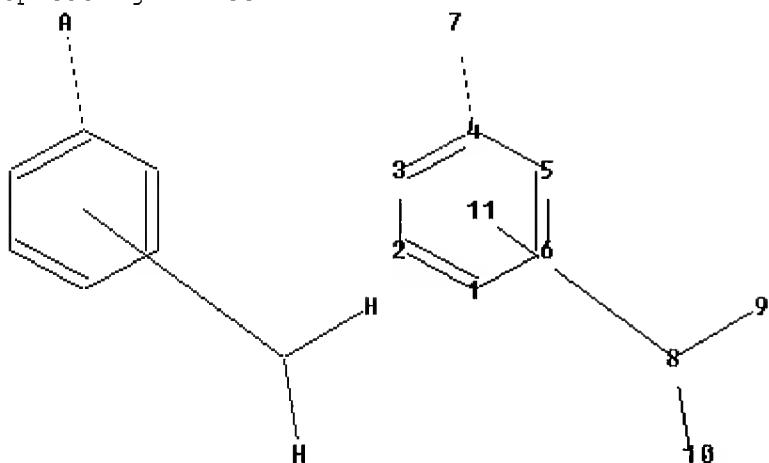
1:
Saturation : Unsaturated
Type of Ring System : Polycyclic
2:
Saturation : Unsaturated
Type of Ring System : Polycyclic

Element Count :

Node 1: Limited
O, O1

Node 2: Limited
S, S1

Uploading L11.str



chain nodes :

8 9 10

ring nodes :

1 2 3 4 5 6 7

chain bonds :

8-9 8-10

ring bonds :

1-2 1-6 2-3 3-4 4-5 4-7 5-6

exact/norm bonds :

4-7

exact bonds :

8-9 8-10

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:CLASS 9:CLASS 10:CLASS
11:CLASS

=> d stat que L24

10/586494

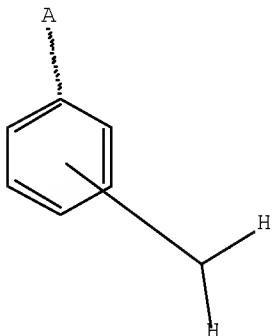
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STR

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Structure attributes must be viewed using STN Express query preparation.

L11 STR



Structure attributes must be viewed using STN Express query preparation.

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L16 SCR 1839

L18 SCR 2005 OR 2021

L20 SCR 1946

L22 2229067 SEA FILE=REGISTRY ABB=ON PLU=ON (C6/ESS (S) (O?/ESS OR S?/ESS)) AND NRS>1 AND NRRS>1

L24 25 SEA FILE=REGISTRY SUB=L22 SSS FUL (L7 AND L11) AND (L15 AND L16 AND L18 AND L20)

100.0% PROCESSED 55623 ITERATIONS
SEARCH TIME: 00.00.02

25 ANSWERS

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=> file zcaplus
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FILE COVERS 1907 - 13 Nov 2008 VOL 149 ISS 20
FILE LAST UPDATED: 12 Nov 2008 (20081112/ED)

ZCAplus now includes complete International Patent Classification (IPC) reclassification data for the second quarter of 2008.

10/586494

New CAS Information Use Policies, enter HELP USAGETERMS for details.

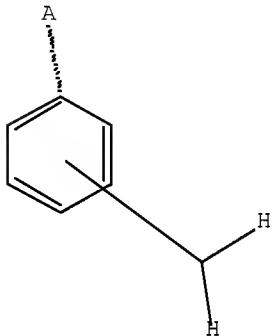
This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'ZCPLUS' FILE

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Structure attributes must be viewed using STN Express query preparation.

L15 SCR 1006 OR 1235
L16 SCR 1839
L18 SCR 2005 OR 2021
L20 SCR 1946
L22 2229067 SEA FILE=REGISTRY ABB=ON PLU=ON (C6/ESS (S) (O?/ESS OR S?/ESS)) AND NRS>1 AND NRRS>1
L24 25 SEA FILE=REGISTRY SUB=L22 SSS FUL (L7 AND L11) AND (L15 AND L16 AND L18 AND L20)
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FILE LAST UPDATED: 12 NOV 2008 <20081112/UP>
MOST RECENT UPDATE: 200873 <200873/DW>
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>>> IPC Reform backfile reclassifications have been loaded to end of September 2008. No update date (UP) has been created for the reclassified documents, but they can be identified by 20060101/UPIC, and 20061231/UPIC, 20070601/UPIC, 20071001/UPIC, 20071130/UPIC, 20080401/UPIC, 20080701/UPIC and 20081001/UPIC.
ECLA reclassifications to mid August and US national classification mid September 2008 have also been loaded. Update dates 20080401,

10/586494

20080701 and 20081001/UPEC and /UPNC have been assigned to these. <<

FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
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EXPLORE DERWENT WORLD PATENTS INDEX IN STN ANAVIST, VERSION 2.0:

http://www.stn-international.com/archive/presentations/DWPIAnaVist2_0608.pdf

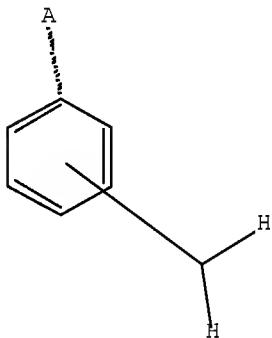
>>> HELP for European Patent Classifications see HELP ECLA, HELP ICO <<<

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Structure attributes must be viewed using STN Express query preparation.
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AND L20)
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=> file beilstein

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FILE LAST UPDATED ON April 1, 2008

FILE COVERS 1771 TO 2008.

*** FILE CONTAINS 10,322,808 SUBSTANCES ***

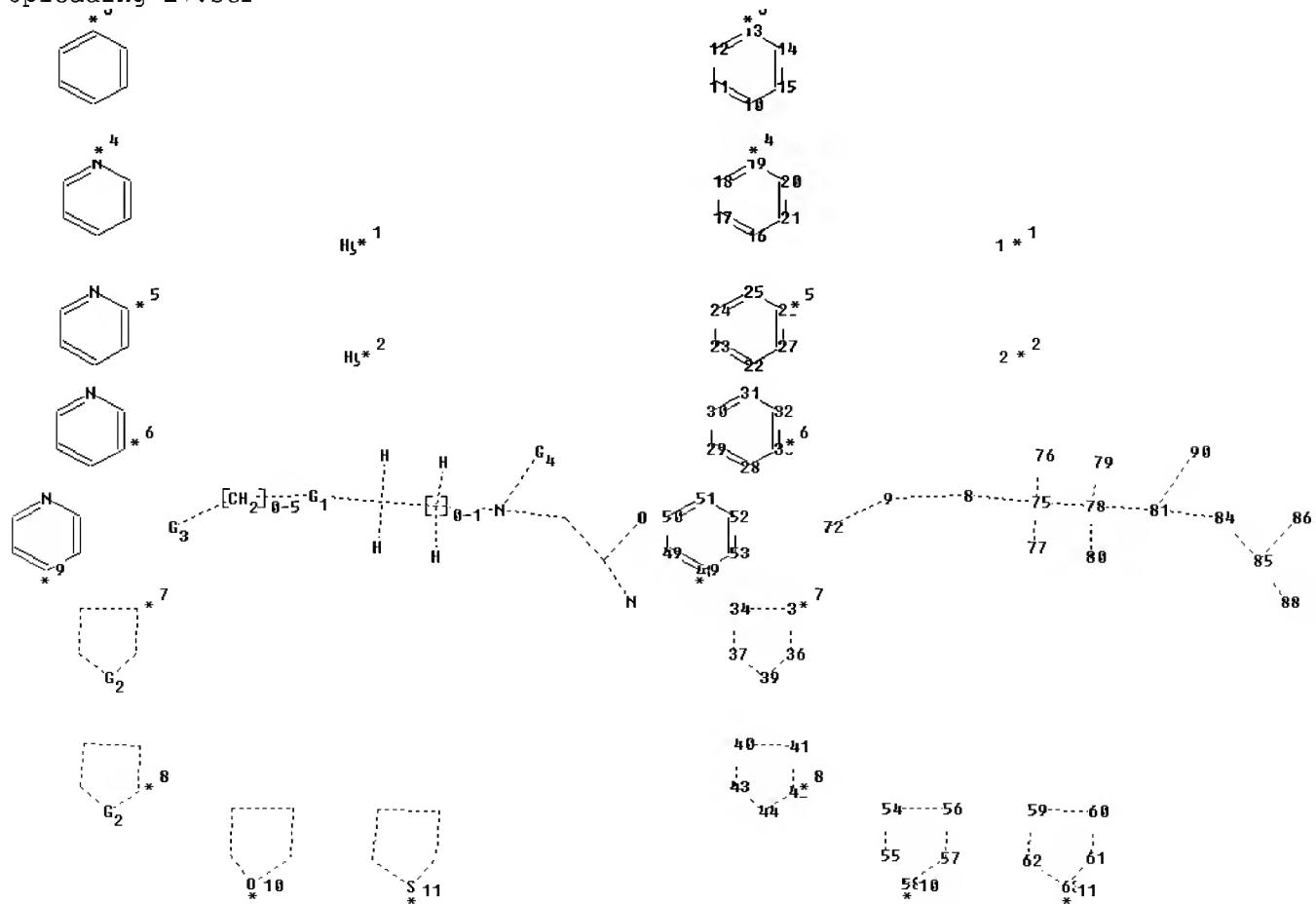
>>> PLEASE NOTE: Reaction Data and substance data are stored in separate documents and can not be searched together in one query. Reaction data for BEILSTEIN compounds may be displayed immediately with the display codes PRE (preparations) and REA (reactions). A substance answer set retrieved after the search for a chemical name, a compounds with available reaction information by combining with PRE/FA, REA/FA or more generally with RX/FA. The BEILSTEIN Registry Number (BRN) is the link between a BEILSTEIN compound and belonging reactions. For more detailed reaction searches BRNs can be searched as reaction partner BRNs Reactant BRN (RX.RBRN) or Product BRN (RX.PBRN).<<<

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>>> Price change as of January 1st, 2008: Connect Time and Structure
 Search fees re-introduced. See NEWS and HELP COST <<<

Uploading L7.str



chain nodes :

10/586494

1 2 8 9 72 75 76 77 78 79 80 81 85 86 90
ring nodes :
10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30
31 32 33 34 35 36 37 39 40 41 42 43 44 48 49 50 51 52 53 54 55
56 57 58
59 60 61 62 63
ring/chain nodes :
84 88
chain bonds :
8-9 8-75 9-72 75-76 75-77 75-78 78-79 78-80 78-81 81-84 81-90 84-85 85-
86
85-88
ring bonds :
10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-21 17-18 18-19 19-20 20-21
22-23 22-27 23-24 24-25 25-26 26-27 28-29 28-33 29-30 30-31 31-32 32-33
34-35 34-37
35-36 36-39 37-39 40-41 40-43 41-42 42-44 43-44 48-49 48-53 49-50 50-51
51-52 52-53
54-55 54-56 55-58 56-57 57-58 59-60 59-62 60-61 61-63 62-63
exact/norm bonds :
8-9 8-75 9-72 34-35 34-37 35-36 36-39 37-39 40-41 40-43 41-42 42-44 43-
44
54-55 54-56 55-58 56-57 57-58 59-60 59-62 60-61 61-63 62-63 75-76 75-77
75-78 78-79
78-80 78-81 81-84 81-90 84-85 85-86 85-88
normalized bonds :
10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-21 17-18 18-19 19-20 20-21
22-23 22-27 23-24 24-25 25-26 26-27 28-29 28-33 29-30 30-31 31-32 32-33
48-49 48-53
49-50 50-51 51-52 52-53

G1:[*1], [*2]

G2:O,S

G3:[*3],[*4],[*5],[*6],[*7],[*8],[*9],[*10],[*11]

G4:H,Cb,Ak

Connectivity :

85:3 E exact RC ring/chain 86:1 E exact RC ring/chain

Match level :

1:Atom 2:Atom 8:CLASS 9:CLASS 10:Atom 11:Atom 12:Atom 13:Atom 14:Atom
15:Atom
16:Atom 17:Atom 18:Atom 19:Atom 20:Atom 21:Atom 22:Atom 23:Atom 24:Atom
25:Atom 26:Atom
27:Atom 28:Atom 29:Atom 30:Atom 31:Atom 32:Atom 33:Atom 34:Atom 35:Atom
36:Atom 37:Atom
39:Atom 40:Atom 41:Atom 42:Atom 43:Atom 44:Atom 48:Atom 49:Atom 50:Atom
51:Atom 52:Atom
53:Atom 54:Atom 55:Atom 56:Atom 57:Atom 58:Atom 59:Atom 60:Atom 61:Atom
62:Atom 63:Atom
72:CLASS 75:CLASS 76:CLASS 77:CLASS 78:CLASS 79:CLASS 80:CLASS 81:CLASS
84:CLASS 85:CLASS
86:CLASS 88:CLASS 90:CLASS

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Type of Ring System : Polycyclic

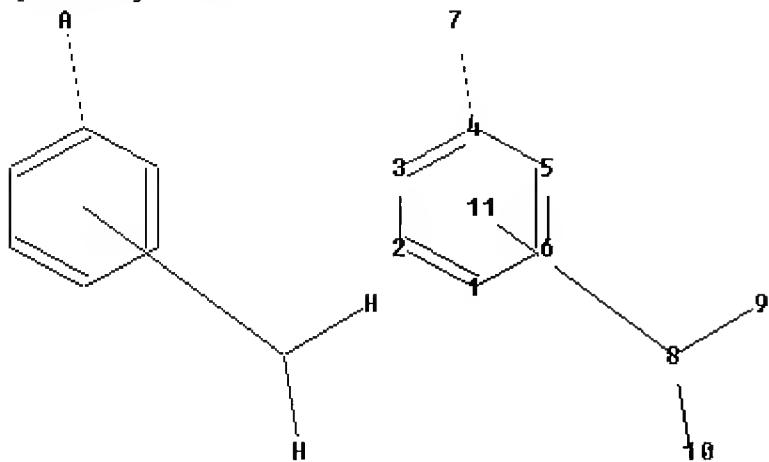
10/586494

2:
Saturation : Unsaturated
Type of Ring System : Polycyclic

Element Count :
Node 1: Limited
0,01

Node 2: Limited
S,S1

Uploading L11.str



chain nodes :
8 9 10
ring nodes :
1 2 3 4 5 6 7
chain bonds :
8-9 8-10
ring bonds :
1-2 1-6 2-3 3-4 4-5 4-7 5-6
exact/norm bonds :
4-7
exact bonds :
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normalized bonds :
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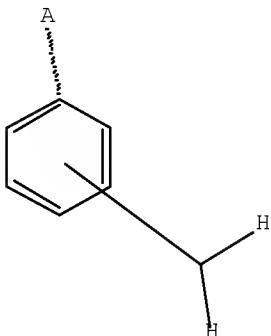
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11:CLASS

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L7 STR

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Structure attributes must be viewed using STN Express query preparation.
L11 STR



Structure attributes must be viewed using STN Express query preparation.
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L16 SCR 1839
L18 SCR 2005 OR 2021
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100.0% PROCESSED 160781 ITERATIONS
SEARCH TIME: 00.01.32

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PROCESSING COMPLETED FOR L25
PROCESSING COMPLETED FOR L33
PROCESSING COMPLETED FOR L28
L48 13 DUP REM L25 L33 L28 (0 DUPLICATES REMOVED)
ANSWER '1' FROM FILE ZCPLUS
ANSWERS '2-5' FROM FILE WPIX
ANSWERS '6-13' FROM FILE BEILSTEIN

=> d ibib abs hitstr L48 1; d iall hitstr L48 2-5; d ide allref L48 6-13

L48 ANSWER 1 OF 13 ZCPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:696729 ZCPLUS Full-text
DOCUMENT NUMBER: 143:179626
TITLE: Alpha-aminoamide derivatives useful in the treatment

INVENTOR(S): of lower urinary tract disorders
 Barbanti, Elena; Veneroni, Orietta; Thaler, Florian;
 Pellicciari, Roberto; Benatti, Luca; Salvati, Patricia
 PATENT ASSIGNEE(S): Newron Pharmaceuticals S.P.A., Italy
 SOURCE: PCT Int. Appl., 42 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005070405	A1	20050804	WO 2005-EP514	20050120
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1557166	A1	20050727	EP 2004-1175	20040121
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AU 2005205903	A1	20050804	AU 2005-205903	20050120
CA 2554047	A1	20050804	CA 2005-2554047	20050120
CN 1956714	A	20070502	CN 2005-80002785	20050120
BR 2005006970	A	20070703	BR 2005-6970	20050120
JP 2007518763	T	20070712	JP 2006-550030	20050120
MX 2006PA08188	A	20061020	MX 2006-PA8188	20060719
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NO 2006003368	A	20061012	NO 2006-3368	20060720
KR 2007007776	A	20070116	KR 2006-714655	20060720
US 20080132567	A1	20080605	US 2007-586494	20070125
PRIORITY APPLN. INFO.:			EP 2004-1175	A 20040121
			US 2003-497722P	P 20030825
			WO 2005-EP514	W 20050120

OTHER SOURCE(S): MARPAT 143:179626

AB The present invention discloses certain α -aminoamide derivs., a chemical class of sodium channel blockers, and their use for treating lower urinary tract disorders and to pharmaceutical compns. containing them. Compds. of the invention include e.g. 2-[(3-phenethyl-2,3-dihydro-benzofuran-5-ylmethyl)-amino]-N-methyl-propanamide. To prepare above compound, a solution of N-methyl-alaninamide hydrochloride 0.50 g in methanol 10 mL, in the presence of mol. sieves 1 g, sodium cyanoborohydride 0.36 g and a solution of 3-(2-phenylethyl)-2,3-dihydro-1-benzofuran-5-carboxaldehyde 0.90 g in methanol 10 mL were added at room temperature. The reaction mixture was kept under stirring and an argon atmospheric for 12 h. Then, the solvent was evaporated under vacuum and purified by flash chromatog. affording 0.93g of 2-[(3-phenethyl-2,3-dihydro-benzofuran-5-ylmethyl)-amino]-N-methyl-propanamide, identified by NMR.

IT 861398-19-3P 861398-20-1P 861398-21-2P
 861398-22-3P 861398-23-4P 861398-24-5P
 861398-25-6P 861398-26-7P 861398-27-8P
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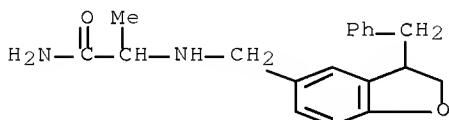
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861398-56-3P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(alpha-aminoamide derivs. useful in treatment of lower urinary tract disorders)

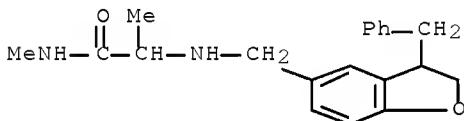
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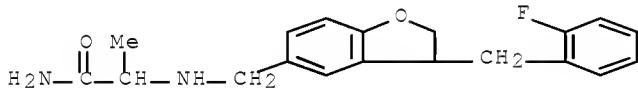
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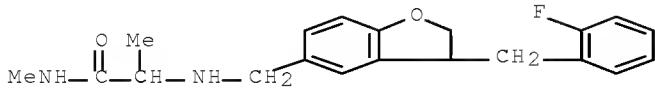
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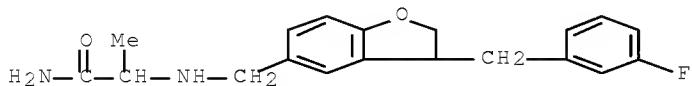
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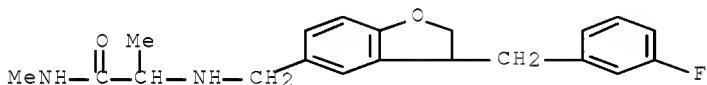
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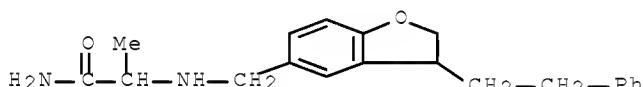
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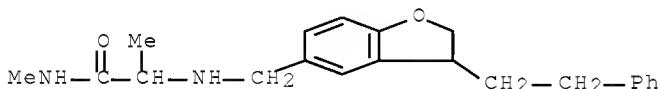
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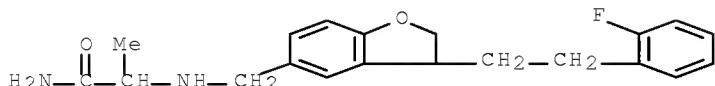
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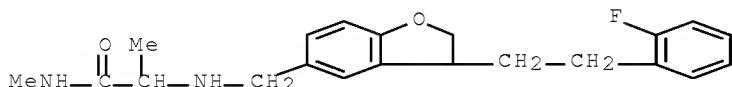
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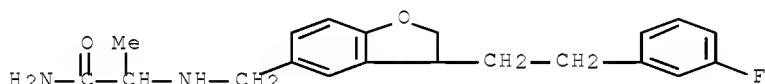
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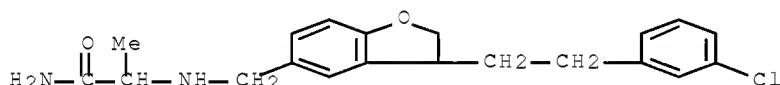
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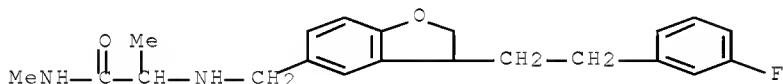
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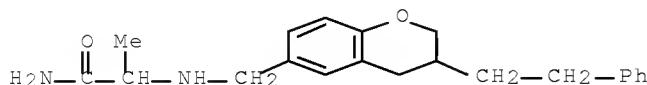
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RN 861398-32-5 ZCPLUS

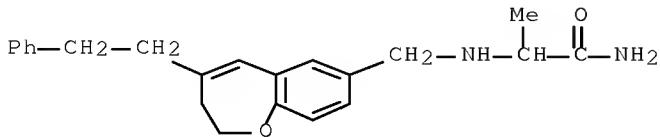
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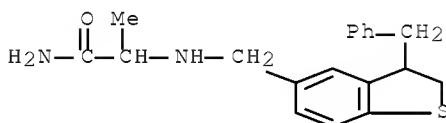
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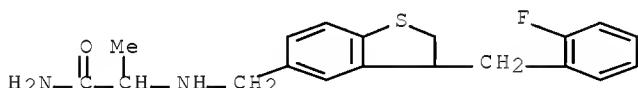
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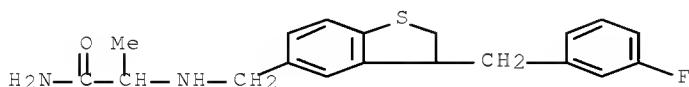
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CN Propanamide, 2-[[3-[(2-fluorophenyl)methyl]-2,3-dihydrobenzo[b]thien-5-yl]methyl]amino]- (CA INDEX NAME)



RN 861398-36-9 ZCPLUS

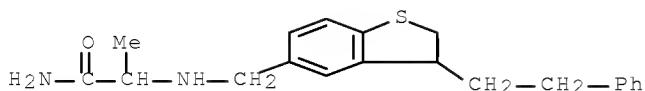
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RN 861398-37-0 ZCPLUS

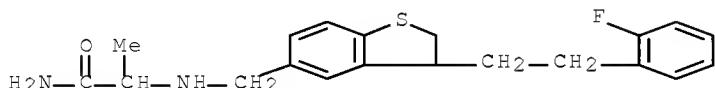
CN Propanamide, 2-[[2,3-dihydro-3-(2-phenylethyl)benzo[b]thien-5-yl]methyl]amino]- (CA INDEX NAME)

10/586494



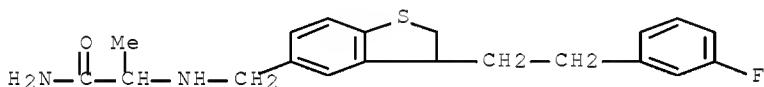
RN 861398-38-1 ZCPLUS

CN Propanamide, 2-[[3-[2-(2-fluorophenyl)ethyl]-2,3-dihydrobenzo[b]thien-5-yl]methyl]amino]- (CA INDEX NAME)



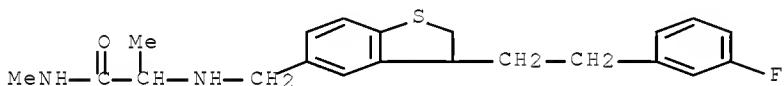
RN 861398-39-2 ZCPLUS

CN Propanamide, 2-[[3-[2-(3-fluorophenyl)ethyl]-2,3-dihydrobenzo[b]thien-5-yl]methyl]amino]- (CA INDEX NAME)



RN 861398-40-5 ZCPLUS

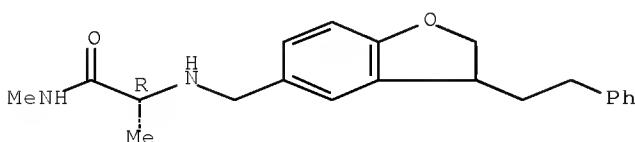
CN Propanamide, 2-[[3-[2-(3-fluorophenyl)ethyl]-2,3-dihydrobenzo[b]thien-5-yl]methyl]amino]-N-methyl- (CA INDEX NAME)



RN 861398-54-1 ZCPLUS

CN Propanamide, 2-[[2,3-dihydro-3-(2-phenylethyl)-5-benzofuranyl]methyl]amino]-N-methyl-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.

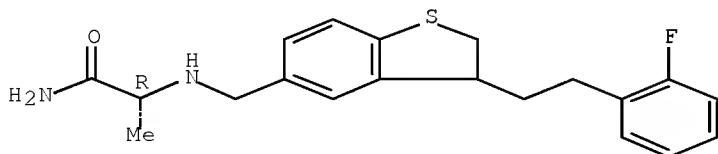


RN 861398-55-2 ZCPLUS

10/586494

CN Propanamide, 2-[3-[2-(2-fluorophenyl)ethyl]-2,3-dihydrobenzo[b]thien-5-yl]methyl]amino]-, (2R)- (CA INDEX NAME)

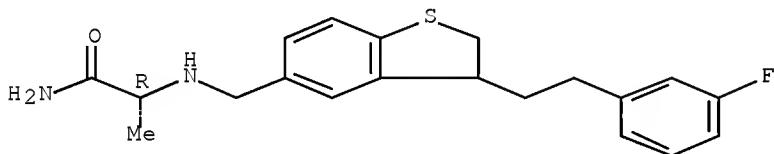
Absolute stereochemistry.



RN 861398-56-3 ZCPLUS

CN Propanamide, 2-[3-[2-(3-fluorophenyl)ethyl]-2,3-dihydrobenzo[b]thien-5-yl]methyl]amino]-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

6

THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L48 ANSWER 2 OF 13 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
ACCESSION NUMBER: 2007-524981 [51] WPIX [Full-text](#)
DOC. NO. CPI: C2007-193716 [51]
TITLE: New diarylimidazole compounds are cannabinoid receptor modulators used for treatment or prophylaxis of e.g. obesity, psychiatric disorders, schizophrenia and bipolar disorders, anxiety, depression, cancer and cognitive disorders
DERWENT CLASS: B03
INVENTOR: AHLQVIST M; CHENG L; LUNDQVIST R; SOERENSEN H; SORENSEN H
PATENT ASSIGNEE: (ASTR-C) ASTRAZENECA AB; (ASTR-C) ASTRAZENECA UK LTD
COUNTRY COUNT: 116

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2007031720	A1	20070322	(200751)*	EN	55[0]	
NO 2008000969	A	20080411	(200832)	NO		
EP 1940803	A1	20080709	(200847)	EN		
IN 2008DN01719	P1	20080627	(200852)	EN		
AU 2006290553	A1	20070322	(200857)	EN		
CN 101263122	A	20080910	(200864)	ZH		
KR 2008048063	A	20080530	(200869)	KO		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2007031720	A1	WO 2006-GB3356	20060912
AU 2006290553	A1	AU 2006-290553	20060912
CN 101263122	A	CN 2006-80033951	20060912
EP 1940803	A1	EP 2006-779372	20060912
NO 2008000969	A PCT Application	WO 2006-GB3356	20060912
EP 1940803	A1 PCT Application	WO 2006-GB3356	20060912
IN 2008DN01719	P1 PCT Application	WO 2006-GB3356	20060912
CN 101263122	A PCT Application	WO 2006-GB3356	20060912
NO 2008000969	A	NO 2008-969	20080226
IN 2008DN01719	P1	IN 2008-DN1719	20080227
KR 2008048063	A PCT Application	WO 2006-GB3356	20060912
KR 2008048063	A	KR 2008-708738	20080411

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1940803	A1	Based on
AU 2006290553	A1	WO 2007031720
CN 101263122	A	WO 2007031720
KR 2008048063	A	WO 2007031720

PRIORITY APPLN. INFO: GB 2005-18817 20050915

INT. PATENT CLASSIFI.:

MAIN: C07D233-90

IPC ORIGINAL: A61K0031-4164 [I,C]; A61K0031-4164 [I,C]; A61K0031-4164 [I,C]; A61K0031-4178 [I,A]; A61K0031-4178 [I,A]; A61P0025-00 [I,A]; A61P0025-00 [I,A]; A61P0025-00 [I,C]; A61P0025-00 [I,C]; C07D0233-00 [I,C]; C07D0233-00 [I,C]; C07D0233-90 [I,A]; C07D0233-90 [I,A]; C07D0401-00 [I,C]; C07D0401-00 [I,C]; C07D0401-00 [I,C]; C07D0401-00 [I,C]; C07D0401-12 [I,A]; C07D0401-12 [I,A]; C07D0409-00 [I,C]; C07D0409-00 [I,C]; C07D0409-00 [I,C]; C07D0409-12 [I,A]; C07D0409-12 [I,A]

ECLA: C07D0233-90; C07D0401-12; C07D0409-12

ICO: M07D0233:90; M07D0401:12; M07D0409:12

BASIC ABSTRACT:

WO 2007031720 A1 UPAB: 20070809

NOVELTY - Diarylimidazole compounds (I) in the form of their methanesulfonate salts (mesylate salt), hemi-1,5-naphthalenedisulfonate salts, hemi-1,2-ethanedisulfonic acid salts, ethylsulfonate salts, nitrate salts, hydrochloride salts, sulfate salts and hydrogen sulfate salts, are new.

DETAILED DESCRIPTION - Diarylimidazole compounds of formula (I) in the form of their methanesulfonate salts (mesylate salts), hemi-1,5-naphthalenedisulfonate salts, hemi-1,2-ethanedisulfonic acid salts, ethylsulfonate salts and nitrate salts, are new.

R1 = 1-10C alkoxy (optionally substituted by F), phenyl(CH₂)_pO (optionally substituted by 1-3 Z), R₅S(O)₂0, R₅S(O)₂NH or (R₆)₃Si;

p = 1-3;

R5 = 1-10C alkyl (optionally substituted by F), or phenyl or heteroaryl (both optionally substituted by 1-3 Z);

R6 = 1-6C alkyl;

Ra = halo 1-3C alkyl or 1-3C alkoxy;

R2 = 1-3C alkyl, 1-3 alkoxy, OH, NO₂, CN or halo;

R2 = 1-3C alkyl, 1-3C alkoxy, OH, NO₂, CN or halo;

R3 = X-Y1-NR7R8;

X = CO or SO2;

Y1 = NH, 1-3C alkyl;

R8 = 1-6C alkyl, 3-15C cycloalkyl, (3-15C cycloalkyl)1-3C alkylene (all optionally substituted by 1-3 W1), (-CH2)r(phenyl)s (optionally substituted by 1-3 Z), saturated 5-8 membered heterocyclic group (containing 1 N and optionally O, S or an additional N and optionally substituted by 1-3C alkyl, OH or benzyl), -(CH2)tHet, where the alkylene chain is optionally substituted by 1-3C alkyl; and

R7 = H or R8; or

NR7R8 = saturated or partially unsaturated 5-8 membered heterocyclic group (containing 1 N and optionally one of O, S or an additional N and optionally substituted by 1-3C alkyl, OH, F or benzyl), oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, pyrrolyl, pyrazolyl, imidazolyl, triazolyl, tetrazolyl, thienyl, furyl or oxazolinyl (all optionally substituted by 1-3 Z);

R4 = H, 1-6C alkyl, 1-6C alkoxy, 1-6C alkoxyl-6C alkylene (which contains a maximum of 6 C atoms and all optionally substituted by F or CN);

Z = 1-3C alkyl, 1-3C alkoxy, OH, halo, -CF3, trifluoromethylthio, difluoromethoxy, -OCF3, trifluoromethylsulfonyl, NO2, amino, mono or di1-3c alkylamino, 1-3C alkylsulfonyl, 1-3C alkoxycarbonyl, carboxy, CN, carbamoyl, mono or di-1-3C alkyl carbamoyl and acetyl;

W1 = OH, F, 1-3C alkyl, 1-3C alkoxy, NH2, mono or di1-3C alkylamino or a heterocyclic amine of morpholinyl, pyrrolidinyl, piperidinyl or piperazinyl in which the heterocyclic amine is optionally substituted by 1-3C alkyl or OH;

m = 0-3;

n = 0-3;

r = 0-4; and

t = 0-4,

provided that r is 0 otherwise s is 1 or 2; when n is 1 then R2 is not -OCH3 in either the 2-position or the 4- position of the phenyl ring; and R1 is not methylsulfonylamino, -OCH3 or CF3O.

ACTIVITY - Anorectic; Neuroleptic; Tranquilizer; Antidepressant; Nootropic; Anabolic; Eating-Disorders-Gen.; Anticonvulsant; Neuroprotective; Antiparkinsonian; Immunomodulator; Cardiovascular-Gen.; Gynecological; Endocrine-Gen.; Antibacterial; Immunosuppressive; Respiratory-Gen.; Gastrointestinal-Gen.; Vasotropic; Antismoking; Hypnotic; Cerebroprotective; Anticoagulant; Analgesic; Antiangular; Antiinfertility; Contraceptive; Antiinflammatory; Hepatotropic; Antiasthmatic; Cytostatic; Antiarthritic.

MECHANISM OF ACTION - Cannabinoid receptor modulator.

In an assay used to determine affinity for central cannabinoid receptors as described in Devane et al, Molecular Pharmacology, 1988, 34,605, using membranes prepared from cells stably transfected with the CB 1 gene, results showed that (I) exhibited IC50 values of less than 200 nm.

USE - Used for the treatment or prophylaxis of obesity, psychiatric disorders such as psychotic disorders, schizophrenia and bipolar disorders, anxiety, anxi-depressive disorders, depression, cognitive disorders, memory disorders, obsessive-compulsive disorders, anorexia, bulimia, attention disorders, epilepsy and related conditions, neurological disorders, Parkinson's disease, Huntington's chorea, Alzheimer's disease, immune, cardiovascular, reproductive and endocrine disorders, septic shock, diseases related to the respiratory and gastrointestinal systems and extended abuse, addiction and/or relapse indications (claimed). (I) are useful e.g. to prevent weight gain, for modulation of appetite and/or satiety, eating disorders, to treat Tourette's syndrome, multiple sclerosis, Raynaud's syndrome, nicotine withdrawal, sleep disorder, cranial trauma, sleep apnea, stroke, cerebral apoplexy, ischemia, cerebral thrombosis, metabolic syndrome, syndrome X, reproductive and endocrine disorders, infertility, contraceptive, gastrointestinal systems, cholelithiasis, asthma, chronic obstructive

pulmonary disease, cancer, Prader-Willi syndrome, arthritis and orthopedic disorders.

ADVANTAGE - (I) are in crystalline form. (I) are more efficacious, less toxic, longer acting, more potent and more easily absorbed. (I) has a broader range of activity, a better pharmacokinetic profile (e.g. higher oral bioavailability and/or lower clearance) and pharmacological, physical or chemical properties. (I) are administered less frequently. (I) exhibits improved ease of handling. (I) may be produced in forms which may have improved chemical and/or solid state stability (e.g. due to lower hygroscopicity). (I) are stable over prolonged periods. (I) are crystallised in good yields, in a high purity and at a low cost. (I) has potency, selectivity profile, half-life in plasma, blood brain permeability, plasma protein binding (higher free fraction of drug) or solubility.

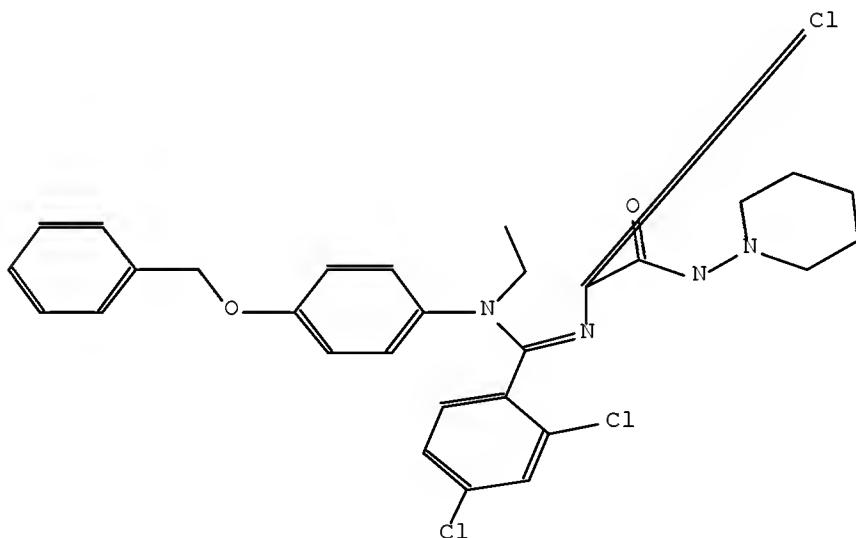
MANUAL CODE:

CPI: B07-D09; B14-C09; B14-D01; B14-E10; B14-E12;
B14-F01; B14-F02; B14-F04; B14-G03; B14-H01; B14-J01;
B14-J02; B14-J07; B14-K01; B14-K01A; B14-L01B; B14-L06B;
B14-M01C; B14-N16; B14-P01; B14-P02; B14-S01; B14-S06;
B14-S07; B14-S13; B14-S16; B14-S20A

AN.S DCR-1502383

CN.S 1-(4-Benzylxy-phenyl)-2-(2,4-dichloro-phenyl)-5-methyl-1H-imidazole-4-carboxylic acid piperidin-1-ylamide hydrochloride

SDCN RAQW9T



L48 ANSWER 3 OF 13 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN

ACCESSION NUMBER: 2006-472374 [48] WPIX [Full-text](#)

DOC. NO. CPI: C2006-148415 [48]

TITLE: New quaternary ammonium salts of fused heteroaromatic amines useful for treating muscarinic acetylcholine receptor mediated disease e.g. chronic obstructive lung disease, chronic bronchitis and asthma

DERWENT CLASS: B02

INVENTOR: BUSCH-PETERSEN J; DAVIS R S; FU W; JIN J; LAINE D I;
PALOVICH M R

PATENT ASSIGNEE: (GLAX-C) GLAXO GROUP LTD

10/586494

COUNTRY COUNT: 111

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2006065755	A2	20060622	(200648)*	EN	33[0]	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2006065755	A2	WO 2005-US44951	20051213

PRIORITY APPLN. INFO: US 2004-635664P 20041213

INT. PATENT CLASSIF.:

IPC ORIGINAL: A61K0031-47 [I,A]; A61K0031-47 [I,C]; A61K0031-4747 [I,A]; A61K0031-4747 [I,C]

BASIC ABSTRACT:

WO 2006065755 A2 UPAB: 20060727

NOVELTY - Quaternary ammonium salts of fused heteroaromatic amines (I) are new.

DETAILED DESCRIPTION - Quaternary ammonium salts of fused heteroaromatic amines of formula R3-T-NH-C(O)-NH-CH(CH2R1)-C(O)-N(R4)-(CH2)n-cyc (I) are new.

cyc=a group of formula (a) or (b);

Y=S, O or NR4;

X and Z=N or CR5;

n=0 - 3;

A=halo, CF3COO, mesylate, tosylate or any other counter ion;

R1=1-8C alkyl, 3-8C cycloalkyl, 3-8C cycloalkyl lower alkyl, 3-8C alkenyl, phenyl (optionally substituted by 1-8C alkoxy, halo, hydroxy, amino, cyano, trifluoromethyl, 1-8C alkyl, 3-8C cycloalkyl, 3-8C cycloalkyl lower alkyl, phenyl or phenyl 1-3C lower alkyl) or phenyl C1-C3 lower alkyl (optionally substituted by 1-8C alkoxy, halo, hydroxy, amino, cyano, trifluoromethyl, 1-8C alkyl, 3-8C cycloalkyl, 3-8C cycloalkyl lower alkyl, phenyl or phenyl 1-3C lower alkyl);

T=thiophene, furan, thiazole, isothiazole, pyrrole, imidazole, pyrazole or para-substituted phenyl (optionally substituted by 1-3C alkoxy, halo, hydroxy, amino, trifluoromethyl, 1-4C alkyl, 3-8C cycloalkyl or 3-8C cycloalkyl lower alkyl or phenyl);

R2=phenyl, naphthyl, phenyl 1-3C lower alkyl (all optionally substituted by 1-8C alkoxy, halo, hydroxy, amino, cyano, trifluoromethyl or 1-3C alkyl), 1-8C alkyl or 3-8C cycloalkyl;

R3=COR6, COOR6, OSO2R6, N(R7)SO2R6, CONR6R7, NR6R7, OCOR6, OCONR6R7, NHCOR6, N(R7)COR6, NHCOOR6 or NHCONR6R7;

R4=H, 1-3C alkyl or allyl;

R5=H, 1-3C alkyl, 2-3C alkenyl, halo, NR4, OR4, CN, NO2 or trifluoromethyl;

R6=1-8C alkyl (optionally substituted by 1-8C alkoxy, halo, hydroxy, amino, cyano, trifluoromethyl or 1-3C alkyl), 3-12C cycloalkyl, 3-12C cycloalkenyl, 3-8C cycloalkyl lower alkyl, 3-8C alkenyl, phenyl or phenyl 1-3C lower alkyl wherein, when substituted, a group is substituted by one or more radicals selected from the group consisting of C1-C3 alkoxy, halo, hydroxy, amino, cyano, nitro, trifluoromethyl, and C1-C3 branched or unbranched alkyl;

R7=H, 1-4C alkyl or allyl.

provided that:

- (1) the number of n at the X value cannot exceed 2; and
- (2) the number of N at the Z value cannot exceed 3

10/586494

ACTIVITY - Respiratory-Gen.; Antiinflammatory; Antiasthmatic;
Antiallergic.

MECHANISM OF ACTION - Muscarinic acetylcholine receptor antagonist.
Efficacy of the compounds (I) to inhibit muscarinic acetylcholine receptor was
determined by 384-well FLIPR assay. Test details are described but no results
are given.

USE - For treating muscarinic acetylcholine receptor mediated disease
such as chronic obstructive lung disease, chronic bronchitis, asthma, chronic
respiratory obstruction, pulmonary fibrosis, pulmonary emphysema and allergic
rhinitis (claimed).

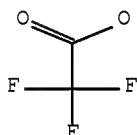
ADVANTAGE - (I) Are capable of causing blockade at M3 muscarinic
acetylcholine receptors; and have a duration of action of at least 24 (preferably
at least 36) hours.

MANUAL CODE: CPI: B06-H; B14-J02B2; B14-K01; B14-N04

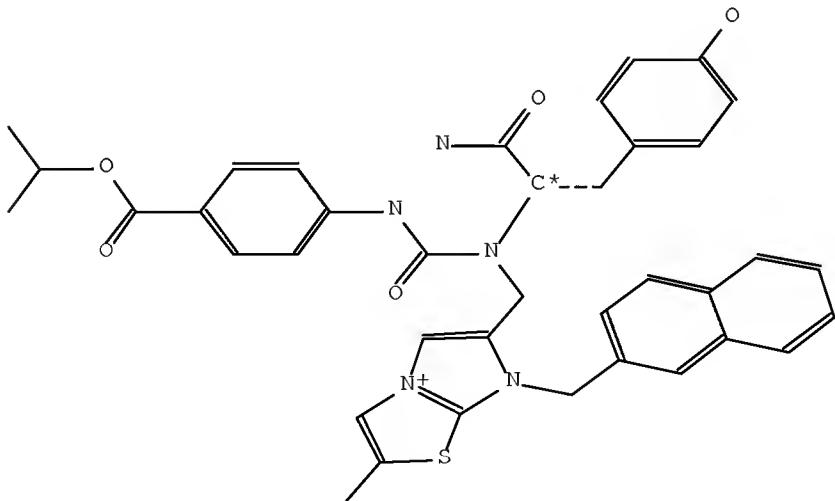
AN.S DCR-1332407

SDCN RAN9TH

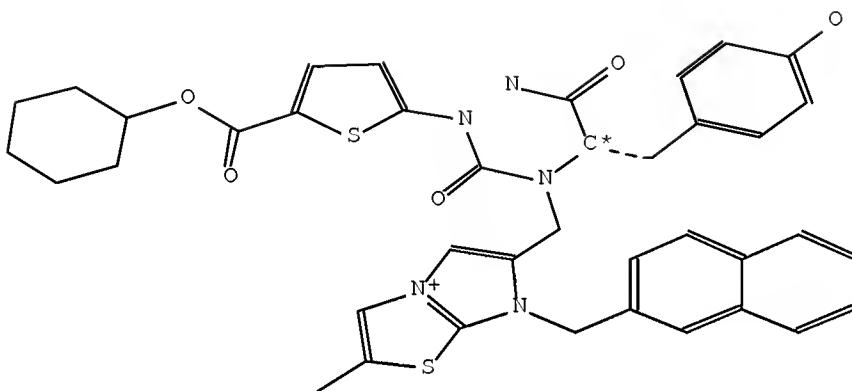
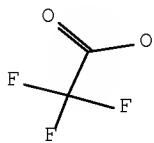
CM 1



CM 2



AN.S DCR-1332408
SDCN RAN9TI



L48 ANSWER 4 OF 13 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
 ACCESSION NUMBER: 2005-417931 [42] WPIX [Full-text](#)
 DOC. NO. CPI: C2005-128203 [42]
 TITLE: New heterocyclic compounds are serine protease inhibitors useful for the treatment or prevention of e.g. arterial and venous thrombosis, ischemic stroke, peripheral arterial disease and acute coronary syndrome
 DERWENT CLASS: B02
 INVENTOR: ANDERLUH M; KIKELJ D; MRAVLJAK J; PECAR S; PREZELJ A;
 SOLLNER DOLENC M; STEFANIC ANDERLUH P; STEGNAR M
 PATENT ASSIGNEE: (LEKT-C) LEK PHARM DD; (UYLJ-N) UNIV LJUBLJANA
 COUNTRY COUNT: 106

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2005051934	A1	20050609	(200542)*	EN	61[0]	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE

10/586494

WO 2005051934 A1

WO 2004-SI40 20041126

PRIORITY APPLN. INFO: SI 2003-287

20031128

INT. PATENT CLASSIF.:

IPC RECLASSIF.: C07D0265-00 [I,C]; C07D0265-36 [I,A]

BASIC ABSTRACT:

WO 2005051934 A1 UPAB: 20051222

NOVELTY - Heterocyclic compounds (I) and their pure enantiomers, mixture of enantiomers, pure diastereomer, mixture of diastereomers or salts are new.

DETAILED DESCRIPTION - Heterocyclic compounds of formula (I) and their pure enantiomers, mixture of enantiomers, pure diastereomer, mixture of diastereomers or salts are new.

A = O, S, NH or CH₂;

B1 = CO or CS;

R1 = H, 1-4C alkyl, benzyl or OR;

R = H, 1-4C alkyl or benzyl;

R2 = H, COOR, CONHR or substituents K1; and

R4 = a substituent bound at position 6 or 7 of the bicyclic and is selected from H, Q-CH(R7)-COOR, Q-CH(R7)CH₂COOR, Q-CH(R7)-CONH-(R9) or M.

For Full Definitions see DEFINITIONS Section.

ACTIVITY - Anticoagulant; Cerebroprotective; Vasotropics; Cardiant; Thrombolytic.

MECHANISM OF ACTION - Serine protease inhibitor.

(I) were tested for their serine protease inhibitory activity using enzyme assay. The results showed that median inhibitory concentration value of (2S)-2-((3-((4-(4-(amino(imino)methyl)benzyl)-3-oxo-3,4-dihydro-2H-1,4-benzoxazin-7-yl)amino)-2-benzyl-3-oxopropanoyl)amino)pentanedioic acid acetate was 0.206 micro-M.

USE - (I) are useful for the inhibition of platelet aggregation caused by fibrinogen, binding to the platelet fibrinogen receptor and simultaneously thrombin inhibition or factor Xa, fibrin formation and blood clots formation.

(I) are useful for the treatment or prevention of arterial and venous thrombosis, ischemic stroke, peripheral arterial disease, acute coronary syndrome, pulmonary embolism or systemic embolism, ischemic complication with surgery e.g. prevention of occlusion in arterial recanalization or blood coagulation in extracorporeal circulation and hemodialysis (all claimed).

ADVANTAGE - (I) are safe and effective. MANUAL CODE: CPI:

B06-D02; B06-D06; B06-E02; B06-F02; B14-D07C;

B14-F01B; B14-F02D; B14-F02D1; B14-F02F3; B14-F04;

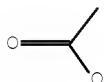
B14-N16

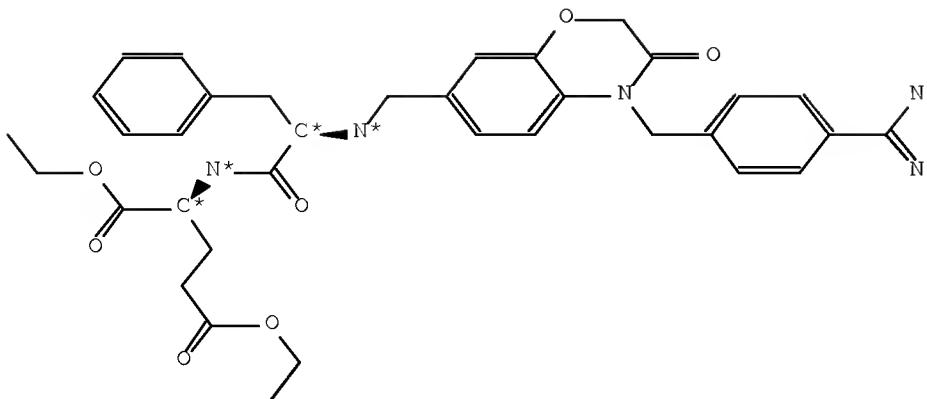
AN.S DCR-1092490

CN.S 2-(2-{[4-(4-Carbamimidoyl-benzyl)-3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-7-ylmethyl]-amino}-3-phenyl-propionylamino)-pentanedioic acid diethyl ester; acetate

SDCN RAI771

CM 1





L48 ANSWER 5 OF 13 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
 ACCESSION NUMBER: 2005-556814 [57] WPIX [Full-text](#)
 DOC. NO. CPI: C2007-041238 [12]
 TITLE: Use of alpha-aminoamide compounds having sodium channel blocking activity for preparation of medicament to treat lower urinary tract disorders e.g. overactive bladder, prostatitis, prostadynia and benign prostatic hyperplasia
 B02; B03
 DERWENT CLASS:
 INVENTOR: BARBANTI E; BENATTI L; PELLICCIARI R; SALVATI P; THALER F; VENERONI O; SAALVATI P
 (NEWR-N) NEWRON PHARM SPA; (BARB-I) BARBANTI E; (BENA-I) BENATTI L; (PELL-I) PELLICCIARI R; (SALV-I) SALVATI P; (THAL-I) THALER F; (VENE-I) VENERONI O
 PATENT ASSIGNEE:
 COUNTRY COUNT: 107

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
EP 1557166	A1	20050727	(200557)*	EN	21[3]	
WO 2005070405	A1	20050804	(200557)	EN		
NO 2006003368	A	20061012	(200675)	NO		
AU 2005205903	A1	20050804	(200707)	EN		
MX 2006008188	A1	20061101	(200737)	ES		
BR 2005006970	A	20070703	(200746)	PT		
JP 2007518763	W	20070712	(200746)	JA	29	
KR 2007007776	A	20070116	(200755)	KO		
CN 1956714	A	20070502	(200760)	ZH		
IN 2006DN04152	P1	20070810	(200780)	EN		
US 20080132567	A1	20080605	(200838)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 1557166 A1		EP 2004-1175	20040121
AU 2005205903 A1		AU 2005-205903	20050120

BR 2005006970 A	BR 2005-6970 20050120
CN 1956714 A	CN 2005-80002785 20050120
WO 2005070405 A1	WO 2005-EP514 20050120
NO 2006003368 A	WO 2005-EP514 20050120
MX 2006008188 A1	WO 2005-EP514 20050120
BR 2005006970 A	WO 2005-EP514 20050120
JP 2007518763 W	WO 2005-EP514 20050120
KR 2007007776 A	WO 2005-EP514 20050120
IN 2006DN04152 P1	WO 2005-EP514 20050120
JP 2007518763 W	JP 2006-550030 20050120
IN 2006DN04152 P1	IN 2006-DN4152 20060719
MX 2006008188 A1	MX 2006-8188 20060719
KR 2007007776 A	KR 2006-714655 20060720
NO 2006003368 A	NO 2006-3368 20060720
US 20080132567 A1	WO 2005-EP514 20050120
US 20080132567 A1	US 2007-586494 20070125

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2005205903	A1	Based on
MX 2006008188	A1	Based on
BR 2005006970	A	Based on
JP 2007518763	W	Based on
KR 2007007776	A	Based on
		WO 2005070405 A

PRIORITY APPLN. INFO: EP 2004-1175 20040121

INT. PATENT CLASSIF.:

MAIN: A61K031-165

IPC ORIGINAL: A61K0031-135 [I,A]; A61K0031-165 [I,A]; A61K0031-165 [I,A]; A61K0031-165 [I,A]; A61K0031-165 [I,C]; A61K0031-165 [I,C]; A61K0031-165 [I,C]; A61K0031-275 [I,C]; A61K0031-277 [I,A]; A61K0031-277 [I,A]; A61K0031-34 [I,A]; A61K0031-34 [I,C]; A61K0031-343 [I,A]; A61K0031-343 [I,A]; A61K0031-343 [I,C]; A61K0031-343 [I,C]; A61K0031-352 [I,C]; A61K0031-353 [I,A]; A61K0031-353 [I,A]; A61K0031-381 [I,A]; A61K0031-381 [I,A]; A61K0031-381 [I,C]; A61K0031-4015 [I,A]; A61K0031-4015 [I,A]; A61K0031-4015 [I,C]; A61K0031-551 [I,A]; A61K0031-551 [I,C]; A61P0013-00 [I,C]; A61P0013-00 [I,C]; A61P0013-00 [I,C]; A61P0013-02 [I,A]; A61P0013-02 [I,A]; A61P0013-02 [I,A]; A61P0013-08 [I,A]; A61P0013-08 [I,A]; A61P0013-10 [I,A]; A61P0013-10 [I,A]; A61P0025-00 [I,C]; A61P0025-04 [I,A]; C07D0307-00 [I,C]; C07D0307-00 [I,C]; C07D0307-00 [I,C]; C07D0307-79 [I,A]; C07D0307-79 [I,A]; C07D0307-79 [I,A]; C07D0311-00 [I,C]; C07D0311-20 [I,A]; C07D0311-20 [I,A]; C07D0313-04 [I,A]; C07D0321-00 [N,C]; C07D0321-10 [N,A]; C07D0333-54 [I,A]

IPC RECLASSIF.: A61K0031-165 [I,A]; A61K0031-165 [I,C]; A61K0031-275 [I,C]; A61K0031-277 [I,A]; A61K0031-34 [I,A]; A61K0031-34 [I,C]; A61K0031-352 [I,C]; A61K0031-353 [I,A]; A61K0031-381 [I,A]; A61K0031-381 [I,C]; A61K0031-4015 [I,A]; A61K0031-4015 [I,C]; C07D0307-00 [I,C]; C07D0307-28 [I,A]; C07D0307-79 [I,A]; C07D0311-00 [I,C]; C07D0311-20 [I,A]; C07D0311-58 [I,A]; C07D0313-00 [I,C]; C07D0313-04 [I,A]; C07D0313-08 [I,A]; C07D0333-00 [I,C];

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 A61K0031-381; A61K0031-4015; C07D0307-28; C07D0311-58;
 C07D0313-08; C07D0333-32; C07D0333-58

ICO: M07D0307:28

USCLASS NCLM: 514/469.000

NCLS: 514/620.000; 549/469.000

BASIC ABSTRACT:

EP 1557166 A1 UPAB: 20070227

NOVELTY - Use of alpha-aminoamide compounds (I) or their isomers, mixtures or salts for the preparation of a medicament to treat lower urinary tract disorders.

DETAILED DESCRIPTION - Use of alpha-aminoamide compounds of formula (I) or their isomers, mixtures or salts for the preparation of a medicament to treat lower urinary tract disorders.

R=furyl, thienyl or pyridyl ring or a phenyl ring (all optionally substituted 1-2 substituents of halo, OH, CN, 1-6C alkyl, 1-6C alkoxy or trifluoromethyl;

R1=H or 1-6C alkyl or 3-7C cycloalkyl; either

R2, R3=H, 1-4C alkyl optionally substituted by OH or phenyl (optionally substituted by 1-2 substituents of 1-6C alkyl, halo, OH, 1-6C alkoxy or trifluoromethyl; or

R2R3C=a 3-6C cycloalkyl ring; either

R4, R5=H, 1-6C alkyl or 3-7C cycloalkyl; or

R4R5N=a 5-7 atom saturated heterocyclic ring;

X=CH₂, O or S; either

Y, Z=H; or

YZ=a 5-7 optionally saturated carbocycle or a heterocycle.

INDEPENDENT CLAIMS are also included for an alpha-aminoamide compound of formula (I); and a composition comprising (I) as an active agent and (I).

ACTIVITY - Uropathic; Antiinflammatory; Cytostatic.

(I) were tested for their ability to treat acute bladder irritation by acetic acid in rats. The results showed that (I) (NW-1029) significantly reversed the acetic acid-induction in the intercontraction intervals in rats.

MECHANISM OF ACTION - Sodium channel blocker.

USE - (I) are useful for the treatment of lower urinary tract disorders (overactive bladder, prostatitis, prostdynia, interstitial cystitis, benign prostatic hyperplasia and urinary incontinence) (claimed).

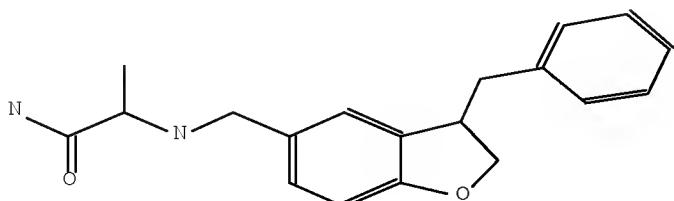
ADVANTAGE - The present invention provides rapid and highly effective methods for treating a variety of lower urinary tract disorders .

MANUAL CODE: CPI: B06-H; B07-H; B10-A15; B10-B02F; B14-H05; B14-L06;
 B14-N07

AN.S DCR-1113141

CN.S 2-[(3-Benzyl-2,3-dihydro-benzofuran-5-ylmethyl)-amino]-propionamide

SDCN RAIMH1

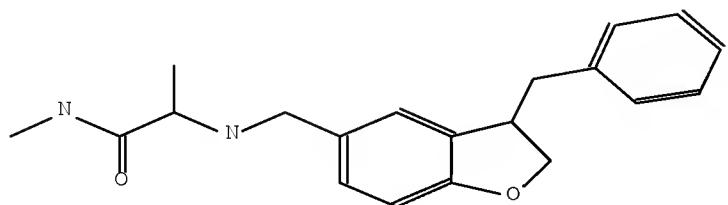


10/586494

AN.S DCR-1113142

CN.S 2-[(3-Benzyl-2,3-dihydro-benzofuran-5-ylmethyl)-amino]-N-methyl-
propionamide

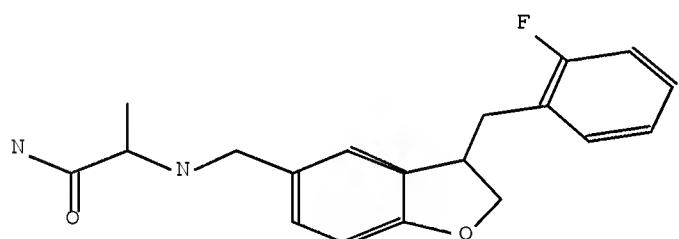
SDCN RAIMH2



AN.S DCR-1113143

CN.S 2-{ [3-(2-Fluoro-benzyl)-2,3-dihydro-benzofuran-5-ylmethyl]-amino } -
propionamide

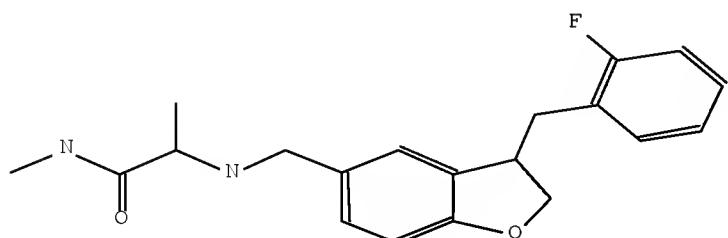
SDCN RAIMH3



AN.S DCR-1113144

CN.S 2-{ [3-(2-Fluoro-benzyl)-2,3-dihydro-benzofuran-5-ylmethyl]-amino } -N-methyl-
propionamide

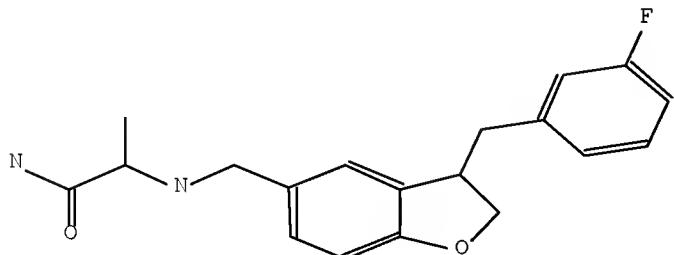
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AN.S DCR-1113145

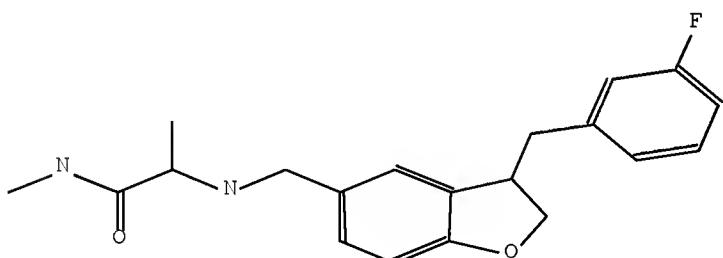
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CN.S 2-{[3-(3-Fluoro-benzyl)-2,3-dihydro-benzofuran-5-ylmethyl]-amino}-propionamide
SDCN RAIMH5



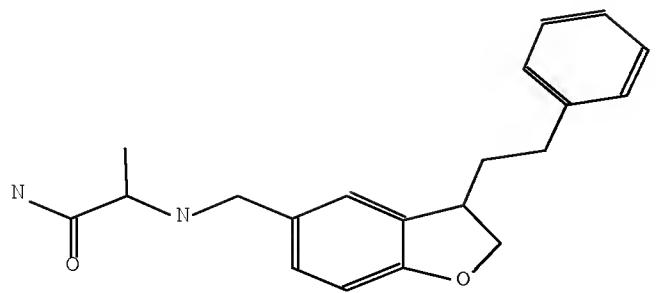
AN.S DCR-1113146

CN.S 2-{[3-(3-Fluoro-benzyl)-2,3-dihydro-benzofuran-5-ylmethyl]-amino}-N-methyl-propionamide
SDCN RAIMH6



AN.S DCR-1113147

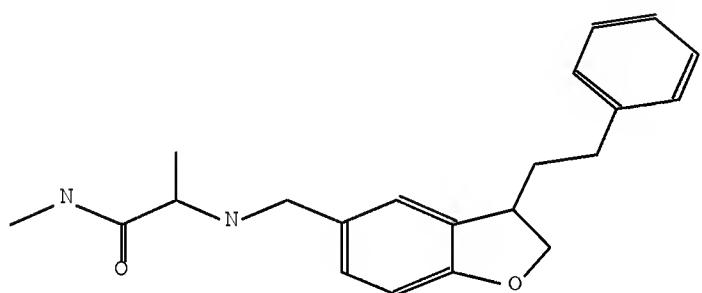
CN.S 2-[(3-Phenethyl-2,3-dihydro-benzofuran-5-ylmethyl)-amino]-propionamide
SDCN RAIMH7



AN.S DCR-1113148

CN.S N-Methyl-2-[(3-phenethyl-2,3-dihydro-benzofuran-5-ylmethyl)-amino]-propionamide

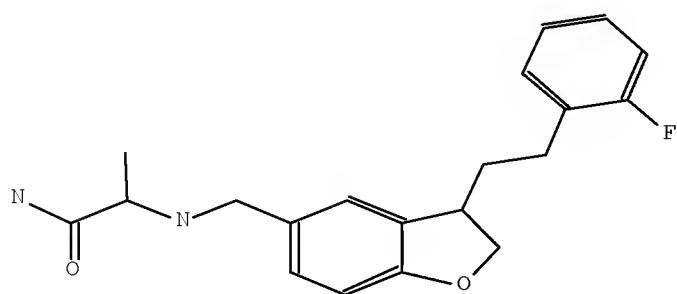
SDCN RAIMH8



AN.S DCR-1113149

CN.S 2-({3- [2-(2-Fluoro-phenyl)-ethyl]-2,3-dihydro-benzofuran-5-ylmethyl}-amino)-propionamide

SDCN RAIMH9

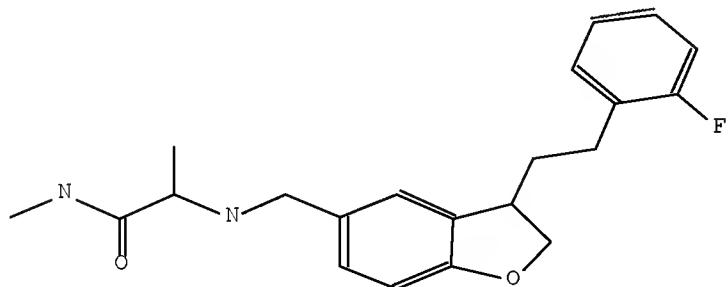


10/586494

AN.S DCR-1113150

CN.S 2-({3-[2-(2-Fluoro-phenyl)-ethyl]-2,3-dihydro-benzofuran-5-ylmethyl}-
amino)-N-methyl-propionamide

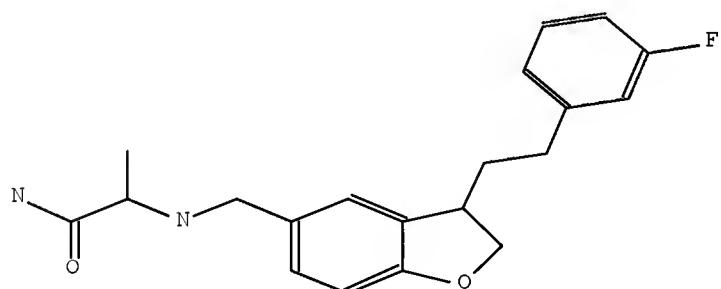
SDCN RAIMHA



AN.S DCR-1113151

CN.S 2-({3-[2-(3-Fluoro-phenyl)-ethyl]-2,3-dihydro-benzofuran-5-ylmethyl}-
amino)-propionamide

SDCN RAIMHB

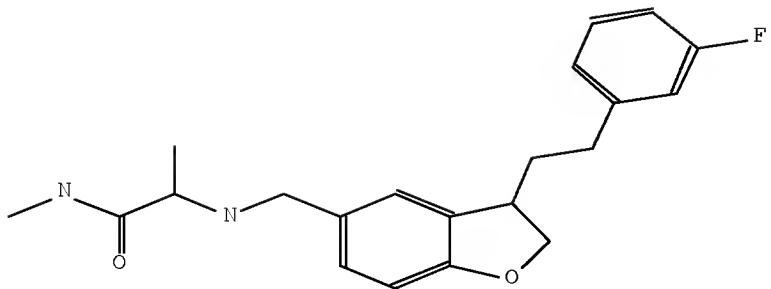


AN.S DCR-1113152

CN.S 2-({3-[2-(3-Fluoro-phenyl)-ethyl]-2,3-dihydro-benzofuran-5-ylmethyl}-
amino)-N-methyl-propionamide

SDCN RAIMHC

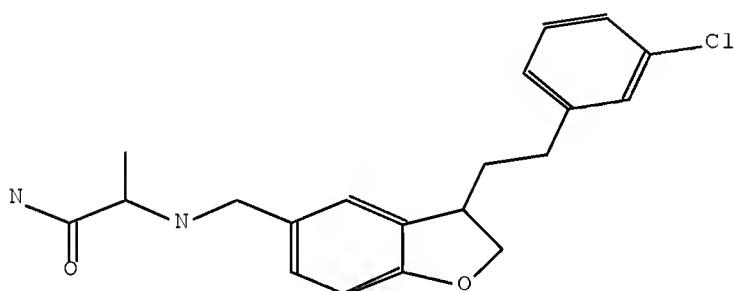
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AN.S DCR-1113153

CN.S 2-({3-[2-(3-Chloro-phenyl)-ethyl]-2,3-dihydro-benzofuran-5-ylmethyl}-amino)-propionamide

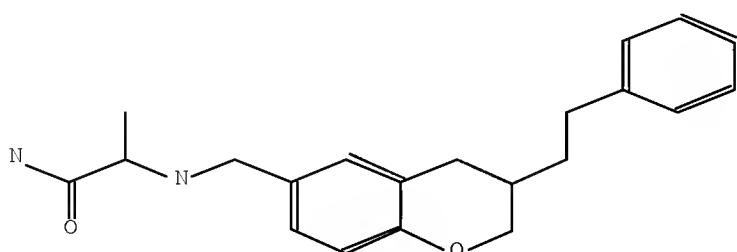
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AN.S DCR-1113154

CN.S 2-[(3-Phenethyl-1-benzopyran-6-ylmethyl)-amino]-propionamide2-[(3-Phenethyl-chroman-6-ylmethyl)-amino]-propionamide

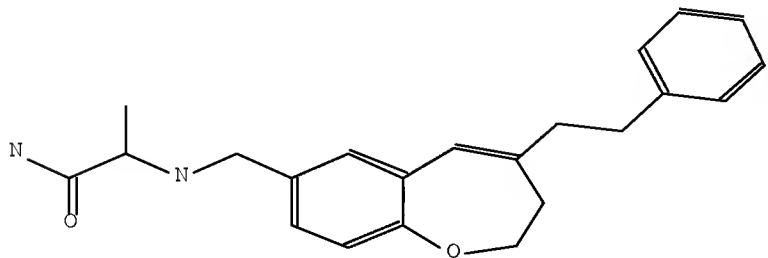
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AN.S DCR-1113155

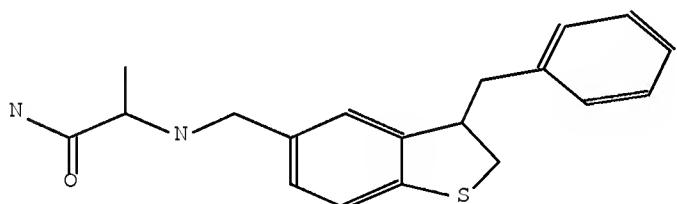
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CN.S 2-[(4-Phenethyl-2,3-dihydro-1-benzoxepin-7-ylmethyl)-amino]-propionamide
[(4-Phenethyl-2,3-dihydro-benzo[b]oxepin-7-ylmethyl)-amino]-propionamide
SDCN RAIMHF



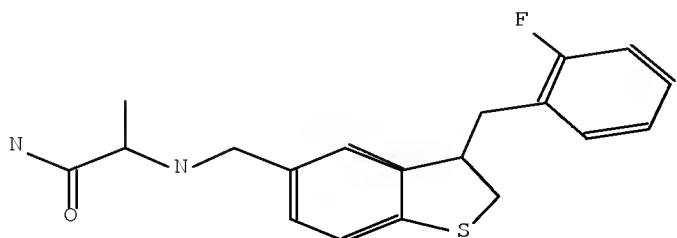
AN.S DCR-1113156

CN.S 2-[(3-Benzyl-2,3-dihydro-benzo[b]thiophen-5-ylmethyl)-amino]-propionamide
SDCN RAIMHG



AN.S DCR-1113157

CN.S 2-{ [3-(2-Fluoro-benzyl)-2,3-dihydro-benzo[b]thiophen-5-ylmethyl]-amino}-
propionamide
SDCN RAIMHH

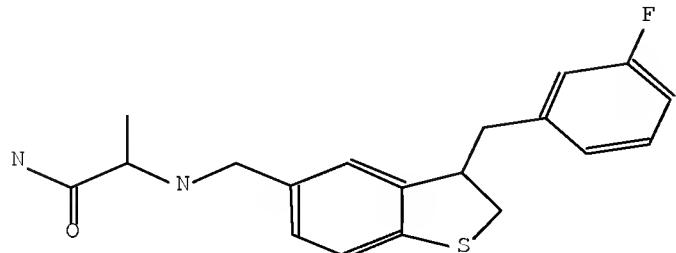


10/586494

AN.S DCR-1113158

CN.S 2-{[3-(3-Fluoro-benzyl)-2,3-dihydro-benzo[b]thiophen-5-ylmethyl]-amino}-propionamide

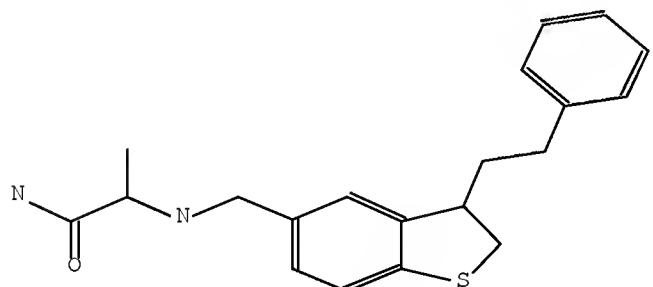
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AN.S DCR-1113159

CN.S 2-[(3-Phenethyl-2,3-dihydro-benzo[b]thiophen-5-ylmethyl)-amino]-propionamide

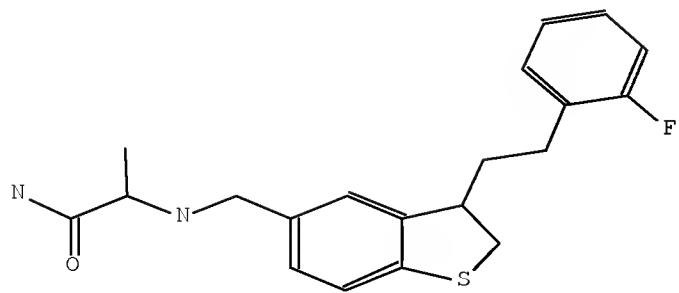
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AN.S DCR-1113160

CN.S 2-({3-[2-(2-Fluoro-phenyl)-ethyl]-2,3-dihydro-benzo[b]thiophen-5-ylmethyl}-amino)-propionamide

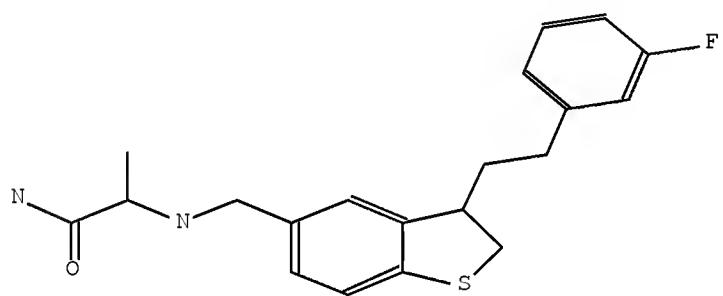
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AN.S DCR-1113161

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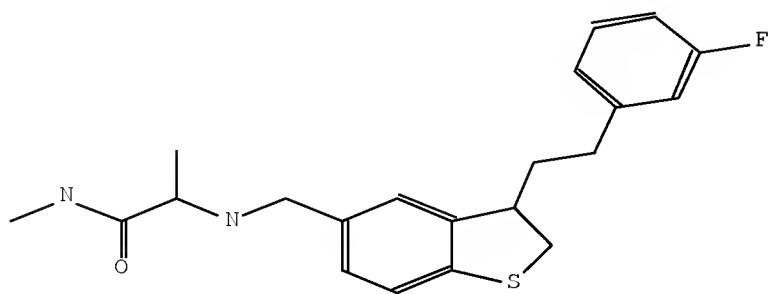
SDCN RAIMHL



AN.S DCR-1113162

CN.S 2-({3-[2-(3-Fluoro-phenyl)-ethyl]-2,3-dihydro-benzo[b]thiophen-5-ylmethyl}-amino)-N-methyl-propionamide

SDCN RAIMHM

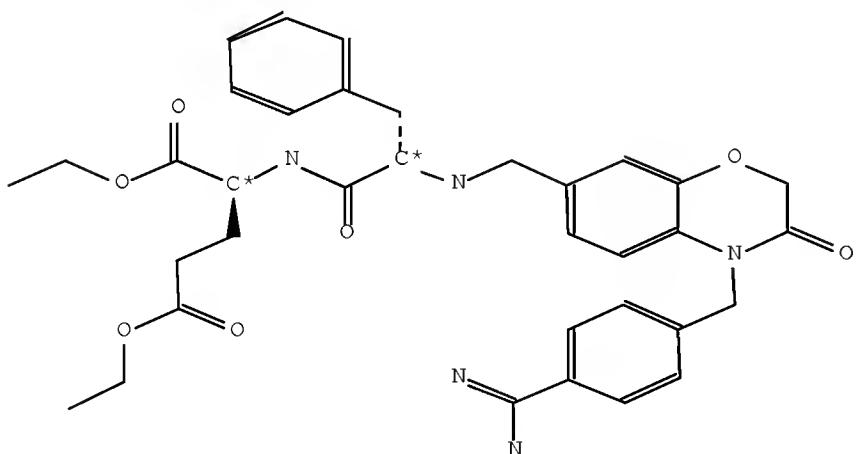


L48 ANSWER 6 OF 13 BEILSTEIN COPYRIGHT 2008 Elsevier Inf. Sys. on STN

Beilstein Records (BRN): 10053555
 Chemical Name (CN): 2-(2-<<4-(4-carbamimidoyl-benzyl)-3-oxo-3,
 4-dihydro-2H-benzo<1,4>oxazin-7-ylmethyl>-
 amino>-3-phenyl-propionylamino)-pentanedio-
 ic acid diethyl ester; compound with
 acetic acid
 Autonom Name (AUN): 2-(2-<<4-(4-carbamimidoyl-benzyl)-3-oxo-3,
 4-dihydro-2H-benzo<1,4>oxazin-7-ylmethyl>-
 amino>-3-phenyl-propionylamino)-pentanedio-
 ic acid diethyl ester; compound with
 acetic acid
 Fragm. Molec. Formula (FMF): C35 H41 N5 O7 , C2 H4 O2
 Molecular Formula (MF): 10 C35 H41 N5 O7 . C2 H4 O2
 Molecular Weight (MW): 643.74, 60.05
 Fragment BRN (FBRN): 10050263, 506007
 Lawson Number (LN): 31661, 16048, 16047, 3488, 1155, 298
 File Segment (FS): Stereo compound
 Compound Type (CTYPE): heterocyclic
 Constitution ID (CONSID): 8456504
 Tautomer ID (TAUTID): 9408488
 Entry Date (DED): 2005/10/20
 Update Date (DUPD): 2005/10/20

CM 1

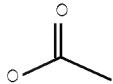
FBRN 10050263
 FMF C35 H41 N5 O7



CM 2

10/586494

FBRN 506007
FMF C2 H4 O2



Field Availability:

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AUN	Autonomname	1
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MF	Molecular Formula	1
FW	Formular Weight	2
FBRN	Fragment BRN	2
LN	Lawson Number	6
FS	File Segment	1
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
DED	Entry Date	1
DUPD	Update Date	1

This substance also occurs in Reaction Documents:

Code	Name	Occurrence
RX	Reaction Documents	1
RXPRO	Substance is Reaction Product	1

All References:

ALLREF

1. Anderluh, Petra Stefanic; Anderluh, Marko; Ilas, Janez; Mravljak, Janez; Dolenc, Marija Sollner; Stegnar, Mojca; Kikelj, Danijel, J. Med. Chem., CODEN: JMCMAR, SIR48(9), <2005>, 3110 - 3113; BABS-6498396

L48 ANSWER 7 OF 13 BEILSTEIN COPYRIGHT 2008 Elsevier Inf. Sys. on STN

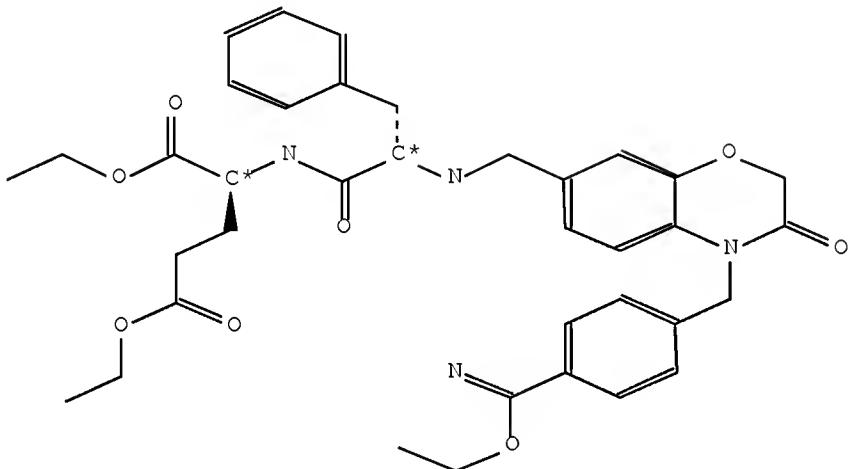
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Autonom Name (AUN):	2-(2-<<4-(4-ethoxycarbonimidoyl-benzyl)-3-oxo-3,4-dihydro-2H-benzo<1,4>oxazin-7-ylmethoxy)-amino>-3-phenyl-propionylamino)-pentanedioic acid diethyl ester; hydrochloride
Fragn. Molec. Formula (FMF):	C37 H44 N4 O8 , Cl H
Molecular Formula (MF):	C37 H44 N4 O8 . Cl H
Molecular Weight (MW):	672.78, 36.46

10/586494

Fragment BRN (FBRN): 10050140, 1098214
Lawson Number (LN): 31661, 16048, 16047, 3488, 298
File Segment (FS): Stereo compound
Compound Type (CTYPE): heterocyclic
Constitution ID (CONSID): 8456175
Tautomer ID (TAUTID): 9407977
Entry Date (DED): 2005/10/20
Update Date (DUPD): 2005/10/20

CM 1

FBRN 10050140
FMF C37 H44 N4 O8



CM 2

FBRN 1098214
FMF C1 H

Field Availability:

Code	Name	Occurrence
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CN	Chemical Name	1
AUN	Autonomname	1
FMF	Fragment Molecular Formula	2
MF	Molecular Formula	1
FW	Formular Weight	2
FBRN	Fragment BRN	2
LN	Lawson Number	5
FS	File Segment	1
CTYPE	Compound Type	1

10/586494

CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
DED	Entry Date	1
DUPD	Update Date	1
PHARM	Pharmacological Data	4

This substance also occurs in Reaction Documents:

Code	Name	Occurrence
RX	Reaction Documents	2
RXREA	Substance is Reaction Reactant	1
RXPRO	Substance is Reaction Product	1

All References:

ALLREF

1. Anderluh, Petra Stefanic; Anderluh, Marko; Ilas, Janez; Mravljak, Janez; Dolenc, Marija Sollner; Stegnar, Mojca; Kikelj, Danijel, J. Med. Chem., CODEN: JMCMAR, SIR48(9), <2005>, 3110 - 3113; BABS-6498396

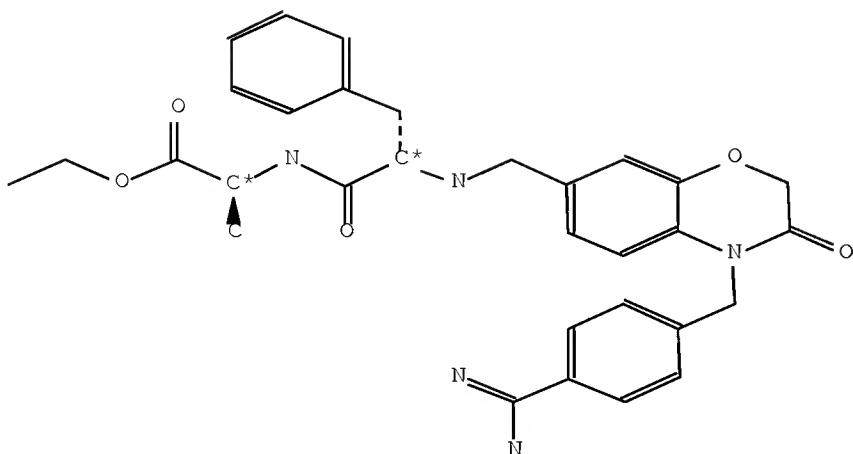
L48 ANSWER 8 OF 13 BEILSTEIN COPYRIGHT 2008 Elsevier Inf. Sys. on STN

Beilstein Records (BRN):	10052187
Chemical Name (CN):	2-(2-<<4-(4-carbamimidoyl-benzyl)-3-oxo-3,4-dihydro-2H-benzo<1,4>oxazin-7-ylmethyl>-amino>-3-phenyl-propionylamino)-propionic acid ethyl ester; compound with acetic acid
Autonom Name (AUN):	2-(2-<<4-(4-carbamimidoyl-benzyl)-3-oxo-3,4-dihydro-2H-benzo<1,4>oxazin-7-ylmethyl>-amino>-3-phenyl-propionylamino)-propionic acid ethyl ester; compound with acetic acid
Fragm. Molec. Formula (FMF):	C31 H35 N5 O5 , C2 H4 O2
Molecular Formula (MF):	C31 H35 N5 O5 . C2 H4 O2
Molecular Weight (MW):	557.65, 60.05
Fragment BRN (FBRN):	10047245, 506007
Lawson Number (LN):	31661, 16048, 16047, 3389, 1155, 298
File Segment (FS):	Stereo compound
Compound Type (CTYPE):	heterocyclic
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Tautomer ID (TAUTID):	9407981
Entry Date (DED):	2005/10/20
Update Date (DUPD):	2005/10/20

CM 1

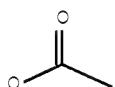
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10/586494



CM 2

FBRN 506007
FMF C2 H4 O2



Field Availability:

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CN	Chemical Name	1
AUN	Autonomname	1
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MF	Molecular Formula	1
FW	Formular Weight	2
FBRN	Fragment BRN	2
LN	Lawson Number	6
FS	File Segment	1
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
DED	Entry Date	1
DUPD	Update Date	1

This substance also occurs in Reaction Documents:

Code	Name	Occurrence
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RX	Reaction Documents	1
RXPRO	Substance is Reaction Product	1

All References:
ALLREF

1. Anderluh, Petra Stefanic; Anderluh, Marko; Ilas, Janez; Mravljak, Janez; Dolenc, Marija Sollner; Stegnar, Mojca; Kikelj, Danijel, J. Med. Chem., CODEN: JMCMAR, SIR48(9), <2005>, 3110 - 3113; BABS-6498396

L48 ANSWER 9 OF 13 BEILSTEIN COPYRIGHT 2008 Elsevier Inf. Sys. on STN

Beilstein Records (BRN):	10051904
Chemical Name (CN):	2-(2-<<4-(4-ethoxycarbonimidoyl-benzyl)-3-oxo-3,4-dihydro-2H-benzo<1,4>oxazin-7-ylmethylethyl>-amino>-3-phenyl-propionylamino)-propionic acid ethyl ester; hydrochloride
Autonom Name (AUN):	2-(2-<<4-(4-ethoxycarbonimidoyl-benzyl)-3-oxo-3,4-dihydro-2H-benzo<1,4>oxazin-7-ylmethylethyl>-amino>-3-phenyl-propionylamino)-propionic acid ethyl ester; hydrochloride
Fragm. Molec. Formula (FMF):	C33 H38 N4 O6 , Cl H
Molecular Formula (MF):	C33 H38 N4 O6 . Cl H
Molecular Weight (MW):	586.69, 36.46
Fragment BRN (FBRN):	10047693, 1098214
Lawson Number (LN):	31661, 16048, 16047, 3389, 298
File Segment (FS):	Stereo compound
Compound Type (CTYPE):	heterocyclic
Constitution ID (CONSID):	8455217
Tautomer ID (TAUTID):	9407385
Entry Date (DED):	2005/10/20
Update Date (DUPD):	2005/10/20

CM 1

FBRN 10047693
FMF C33 H38 N4 O6

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

CM 2

FBRN 1098214
FMF Cl H

Field Availability:

Code	Name	Occurrence
BRN	Beilstein Records	1
CN	Chemical Name	1
AUN	Autonomname	1
FMF	Fragment Molecular Formula	2
MF	Molecular Formula	1
FW	Formular Weight	2
FBRN	Fragment BRN	2

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LN	Lawson Number	5
FS	File Segment	1
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
DED	Entry Date	1
DUPD	Update Date	1

This substance also occurs in Reaction Documents:

Code	Name	Occurrence
RX	Reaction Documents	2
RXREA	Substance is Reaction Reactant	1
RXPRO	Substance is Reaction Product	1

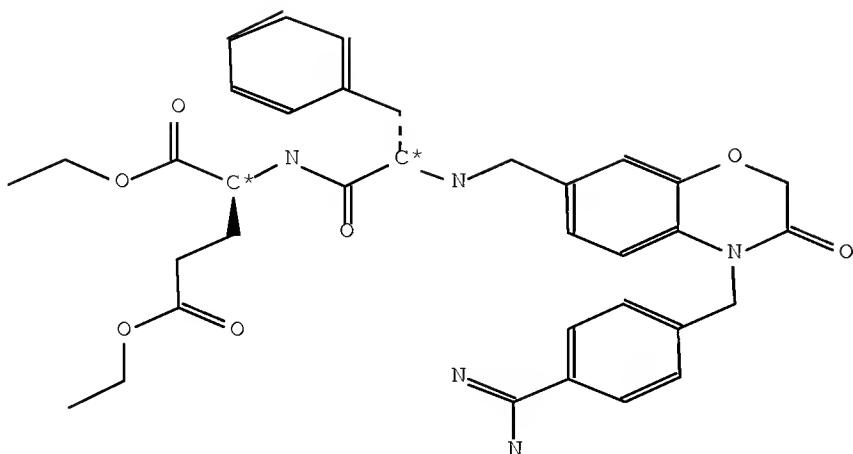
All References:

ALLREF

1. Anderluh, Petra Stefanic; Anderluh, Marko; Ilas, Janez; Mravljak, Janez; Dolenc, Marija Sollner; Stegnar, Mojca; Kikelj, Danijel, J. Med. Chem., CODEN: JMCMAR, SIR48(9), <2005>, 3110 - 3113; BABS-6498396

L48 ANSWER 10 OF 13 BEILSTEIN COPYRIGHT 2008 Elsevier Inf. Sys. on STN

Beilstein Records (BRN):	10050263
Chemical Name (CN):	2-(2-<<4-(4-carbamimidoyl-benzyl)-3-oxo-3, 4-dihydro-2H-benzo<1,4>oxazin-7-ylmethyl>- amino>-3-phenyl-propionylamino)-pentanedio ic acid diethyl ester
Autonom Name (AUN):	2-(2-<<4-(4-carbamimidoyl-benzyl)-3-oxo-3, 4-dihydro-2H-benzo<1,4>oxazin-7-ylmethyl>- amino>-3-phenyl-propionylamino)-pentanedio ic acid diethyl ester
Molec. Formula (MF):	C35 H41 N5 O7
Molecular Weight (MW):	643.74
Lawson Number (LN):	31661, 16048, 16047, 3488, 298
File Segment (FS):	Stereo compound
Compound Type (CTYPE):	heterocyclic
Constitution ID (CONSID):	8453461
Tautomer ID (TAUTID):	9406763
Entry Date (DED):	2005/10/20
Update Date (DUPD):	2005/10/20



Field Availability:

Code	Name	Occurrence
BRN	Beilstein Records	1
CN	Chemical Name	1
AUN	Autonomname	1
LSF	Linearized Structure Formula	1
MF	Molecular Formula	1
FW	Formular Weight	1
FBRN	Fragment BRN	2
LN	Lawson Number	5
FS	File Segment	1
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
DED	Entry Date	1
DUPD	Update Date	1
CDER	Chemical Derivative	1
PHARM	Pharmacological Data	4

All References:

ALLREF

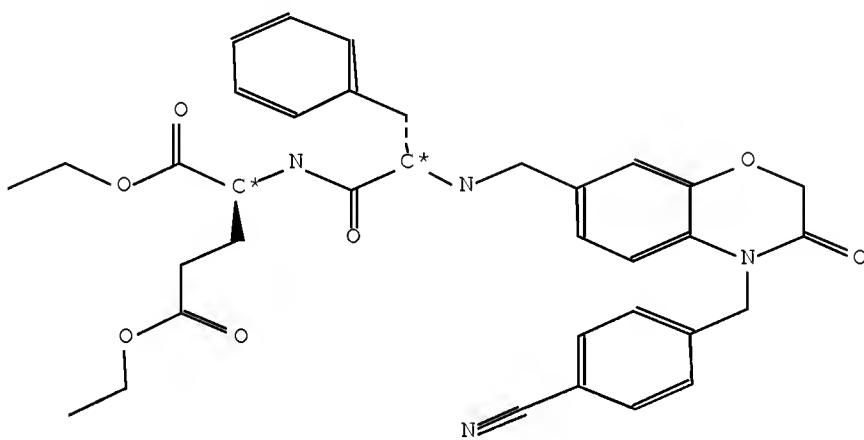
1. Anderluh, Petra Stefanic; Anderluh, Marko; Ilas, Janez; Mravljak, Janez; Dolenc, Marija Sollner; Stegnar, Mojca; Kikelj, Danijel, J. Med. Chem., CODEN: JMCMAR, SIR48(9), <2005>, 3110 - 3113; BABS-6498396

L48 ANSWER 11 OF 13 BEILSTEIN COPYRIGHT 2008 Elsevier Inf. Sys. on STN

Beilstein Records (BRN): 10049305
 Chemical Name (CN): 2-(2-<<4-(4-cyano-benzyl)-3-oxo-3,4-dihydro-2H-benzol[1,4]oxazin-7-ylmethyl>-amino>-3-phenyl-propionylamino)-pentanedioic acid diethyl ester
 Autonom Name (AUN): 2-(2-<<4-(4-cyano-benzyl)-3-oxo-3,4-dihydro-2H-benzol[1,4]oxazin-7-ylmethyl>-amino>-3-phenyl-propionylamino)-pentanedioic acid

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Molec. Formula (MF):	diethyl ester
Molecular Weight (MW):	C35 H38 N4 O7
Lawson Number (LN):	626.71
File Segment (FS):	31661, 16048, 16046, 3488, 298
Compound Type (CTYPE):	Stereo compound
Constitution ID (CONSID):	heterocyclic
Tautomer ID (TAUTID):	8452600
Entry Date (DED):	9406716
Update Date (DUPD):	2005/10/20
	2005/10/20



Field Availability:

Code	Name	Occurrence
BRN	Beilstein Records	1
CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	5
FS	File Segment	1
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
DED	Entry Date	1
DUPD	Update Date	1

This substance also occurs in Reaction Documents:

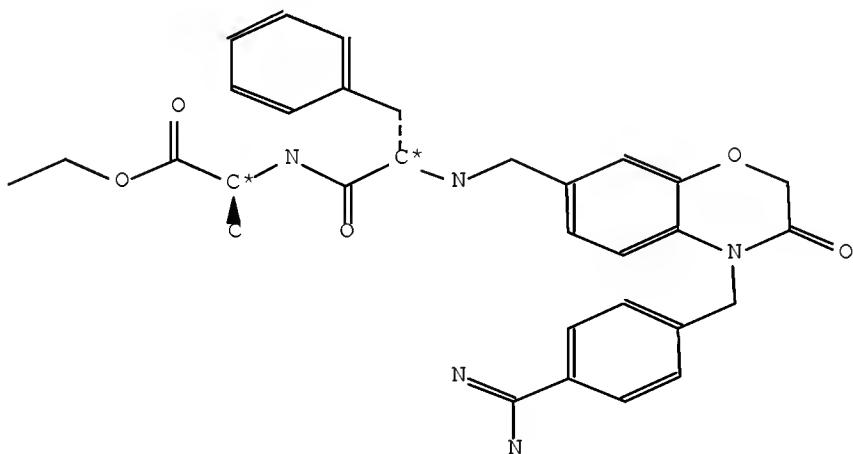
Code	Name	Occurrence
RX	Reaction Documents	2
RXREA	Substance is Reaction Reactant	1
RXPRO	Substance is Reaction Product	1

All References:
ALLREF

1. Anderluh, Petra Stefanic; Anderluh, Marko; Ilas, Janez; Mravljak, Janez; Dolenc, Marija Sollner; Stegnar, Mojca; Kikelj, Danijel, J. Med. Chem., CODEN: JMCMAR, SIR48(9), <2005>, 3110 - 3113; BABS-6498396

L48 ANSWER 12 OF 13 BEILSTEIN COPYRIGHT 2008 Elsevier Inf. Sys. on STN

Beilstein Records (BRN):	10047245
Chemical Name (CN):	2-(2-<<4-(4-carbamimidoyl-benzyl)-3-oxo-3,4-dihydro-2H-benzo<1,4>oxazin-7-ylmethyl>-amino>-3-phenyl-propionylamino)-propionic acid ethyl ester
Autonom Name (AUN):	2-(2-<<4-(4-carbamimidoyl-benzyl)-3-oxo-3,4-dihydro-2H-benzo<1,4>oxazin-7-ylmethyl>-amino>-3-phenyl-propionylamino)-propionic acid ethyl ester
Molec. Formula (MF):	C31 H35 N5 O5
Molecular Weight (MW):	557.65
Lawson Number (LN):	31661, 16048, 16047, 3389, 298
File Segment (FS):	Stereo compound
Compound Type (CTYPE):	heterocyclic
Constitution ID (CONSID):	8450672
Tautomer ID (TAUTID):	9405921
Entry Date (DED):	2005/10/20
Update Date (DUPD):	2005/10/20



Field Availability:

Code	Name	Occurrence
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BRN	Beilstein Records	1
CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1

FW	Formular Weight	1
LN	Lawson Number	5
FS	File Segment	1
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
DED	Entry Date	1
DUPD	Update Date	1
PHARM	Pharmacological Data	4

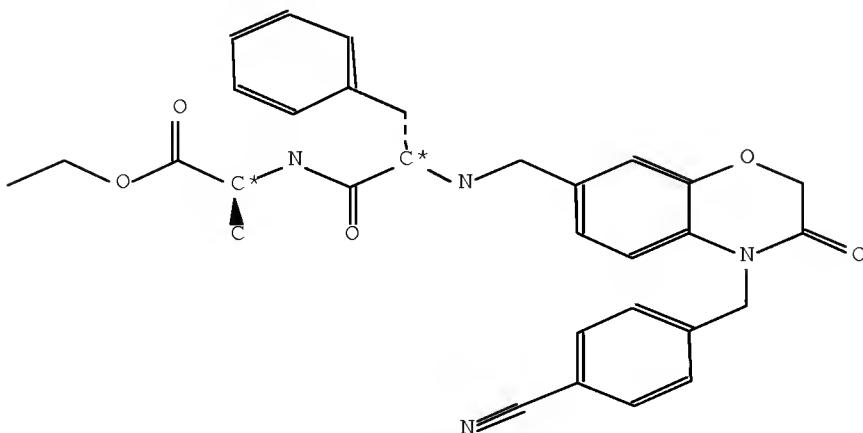
All References:

ALLREF

1. Anderluh, Petra Stefanic; Anderluh, Marko; Ilas, Janez; Mravljak, Janez; Dolenc, Marija Sollner; Stegnar, Mojca; Kikelj, Danijel, J. Med. Chem., CODEN: JMCMAR, SIR48(9), <2005>, 3110 - 3113; BABS-6498396

L48 ANSWER 13 OF 13 BEILSTEIN COPYRIGHT 2008 Elsevier Inf. Sys. on STN

Beilstein Records (BRN):	10045499
Chemical Name (CN):	2-(2-<<4-(4-cyano-benzyl)-3-oxo-3,4-dihydro-2H-benzo<1,4>oxazin-7-ylmethyl>-amino>-3-phenyl-propionylamino)-propionic acid ethyl ester
Autonom Name (AUN):	2-(2-<<4-(4-cyano-benzyl)-3-oxo-3,4-dihydro-2H-benzo<1,4>oxazin-7-ylmethyl>-amino>-3-phenyl-propionylamino)-propionic acid ethyl ester
Molec. Formula (MF):	C31 H32 N4 O5
Molecular Weight (MW):	540.62
Lawson Number (LN):	31661, 16048, 16046, 3389, 298
File Segment (FS):	Stereo compound
Compound Type (CTYPE):	heterocyclic
Constitution ID (CONSID):	8449063
Tautomer ID (TAUTID):	9405693
Entry Date (DED):	2005/10/20
Update Date (DUPD):	2005/10/20



Field Availability:

Code	Name	Occurrence
BRN	Beilstein Records	1
CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	5
FS	File Segment	1
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
DED	Entry Date	1
DUPD	Update Date	1

This substance also occurs in Reaction Documents:

Code	Name	Occurrence
RX	Reaction Documents	2
RXREA	Substance is Reaction Reactant	1
RXPRO	Substance is Reaction Product	1

All References:

ALLREF

1. Anderluh, Petra Stefanic; Anderluh, Marko; Ilas, Janez; Mravljak, Janez; Dolenc, Marija Sollner; Stegnar, Mojca; Kikelj, Danijel, J. Med. Chem., CODEN: JMCMAR, SIR48(9), <2005>, 3110 – 3113; BABS-6498396

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=> d his full

(FILE 'HOME' ENTERED AT 15:17:26 ON 13 NOV 2008)

FILE 'ZCAPLUS' ENTERED AT 15:17:58 ON 13 NOV 2008

E US2006-586494 /APPS

L1 1 SEA ABB=ON PLU=ON US2006-586494 /AP
D SCA
L2 1 SEA ABB=ON PLU=ON US2007-586494 /AP
D SCA
SEL RN

FILE 'REGISTRY' ENTERED AT 15:19:13 ON 13 NOV 2008

L3 101 SEA ABB=ON PLU=ON (109209-65-6/BI OR 133865-35-7/BI OR
133865-72-2/BI OR 133865-78-8/BI OR 133865-88-0/BI OR 133865-89
-1/BI OR 133866-09-8/BI OR 133866-10-1/BI OR 133866-11-2/BI OR
133866-12-3/BI OR 133866-14-5/BI OR 133866-15-6/BI OR 133866-18
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133866-27-0/BI OR 15126-07-5/BI OR 155295-66-2/BI OR 166949-64-
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-3/BI OR 230288-01-4/BI OR 230288-02-5/BI OR 230288-04-7/BI OR
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-6/BI OR 861398-60-9/BI OR 861398-61-0/BI OR 861398-62-1/BI OR
861398-63-2/BI)
L4 31 SEA ABB=ON PLU=ON L3 AND NRRS>1
L5 25 SEA ABB=ON PLU=ON L4 AND N>1

FILE 'ZCAPLUS' ENTERED AT 15:27:00 ON 13 NOV 2008

L6 1 SEA ABB=ON PLU=ON L5

FILE 'REGISTRY' ENTERED AT 15:51:35 ON 13 NOV 2008

L7 STRUCTURE UPLOADED
L8 1 SEA SSS SAM L7
D SCA
L9 STRUCTURE UPLOADED
L10 0 SEA SSS SAM L7 AND L9
L11 STRUCTURE UPLOADED
L12 0 SEA SSS SAM L7 AND L11
L13 SCREEN 1006

10/586494

L14 SCREEN 1235
L15 SCREEN 1006 OR 1235
L16 SCREEN 1839
L17 0 SEA SSS SAM (L7 AND L11) AND (L15 AND L16)
L18 SCREEN 2005 OR 2021
L19 0 SEA SSS SAM (L7 AND L11) AND (L15 AND L16 AND L18)
L20 SCREEN 1946
L21 0 SEA SSS SAM (L7 AND L11) AND (L15 AND L16 AND L18 AND L20)
L*** DEL 0 S C6/ESS AND NRRS>1 AND NRS>1 AND C>11 AND (O/RELS OR S/RELS)
L22 2229067 SEA ABB=ON PLU=ON (C6/ESS (S) (O?/ESS OR S?/ESS)) AND NRS>1
AND NRRS>1
L23 2 SEA SUB=L22 SSS SAM (L7 AND L11) AND (L15 AND L16 AND L18 AND
L20)
D SCA
L24 25 SEA SUB=L22 SSS FUL (L7 AND L11) AND (L15 AND L16 AND L18 AND
L20)
SAVE TEMP L24 ST0494L7L11/A

FILE 'ZCAPLUS' ENTERED AT 16:11:49 ON 13 NOV 2008
L25 1 SEA ABB=ON PLU=ON L24

FILE 'REGISTRY' ENTERED AT 16:12:08 ON 13 NOV 2008
L26 25 SEA ABB=ON PLU=ON L24 AND L5

FILE 'BEILSTEIN' ENTERED AT 16:17:11 ON 13 NOV 2008
L27 1 SEA SSS SAM (L7 AND L11) AND (L15 AND L16 AND L18 AND L20)
L28 8 SEA SSS FUL (L7 AND L11) AND (L15 AND L16 AND L18 AND L20)
L29 8 SEA ABB=ON PLU=ON L28/COM
L30 3 SEA ABB=ON PLU=ON L29 AND BABSAN/FA

FILE 'WPIX' ENTERED AT 16:20:24 ON 13 NOV 2008
L31 0 SEA SSS SAM (L7 AND L11) AND (L15 AND L16 AND L18 AND L20)
L32 26 SEA SSS FUL (L7 AND L11) AND (L15 AND L16 AND L18 AND L20)
L33 4 SEA ABB=ON PLU=ON L32/DCR

FILE 'ZCAPLUS' ENTERED AT 16:22:08 ON 13 NOV 2008
L34 17 SEA ABB=ON PLU=ON BARBANTI E?/AU
L35 11 SEA ABB=ON PLU=ON VENERONI O?/AU
L36 31 SEA ABB=ON PLU=ON THALER F?/AU
L37 287 SEA ABB=ON PLU=ON PELLICCIARI R?/AU
L38 51 SEA ABB=ON PLU=ON BENATTI L?/AU
L39 111 SEA ABB=ON PLU=ON SALVATI P?/AU
L40 5 SEA ABB=ON PLU=ON L34 AND (L35 OR L36 OR L37 OR L38 OR L39)
L41 7 SEA ABB=ON PLU=ON L35 AND (L36 OR L37 OR L38 OR L39)
L42 8 SEA ABB=ON PLU=ON L36 AND (L37 OR L38 OR L39)
L43 3 SEA ABB=ON PLU=ON L37 AND (L38 OR L39)
L44 10 SEA ABB=ON PLU=ON L38 AND L39
L45 20 SEA ABB=ON PLU=ON (L40 OR L41 OR L42 OR L43 OR L44)

FILE 'MEDLINE, EMBASE, BIOSIS, WPIX' ENTERED AT 16:24:08 ON 13 NOV 2008
L46 39 SEA ABB=ON PLU=ON L45

FILE 'ZCAPLUS' ENTERED AT 16:24:22 ON 13 NOV 2008
D STAT QUE L45

FILE 'MEDLINE, EMBASE, BIOSIS, WPIX' ENTERED AT 16:24:31 ON 13 NOV 2008
D STAT QUE L46

FILE 'ZCAPLUS, MEDLINE, EMBASE, BIOSIS, WPIX' ENTERED AT 16:24:43 ON 13
NOV 2008

10/586494

L47 34 DUP REM L45 L46 (25 DUPLICATES REMOVED)
 ANSWERS '1-20' FROM FILE ZCPLUS
 ANSWER '21' FROM FILE MEDLINE
 ANSWERS '22-32' FROM FILE BIOSIS
 ANSWERS '33-34' FROM FILE WPIX
D IBIB ABS L47 1-20
D IALL L47 21-34

FILE 'REGISTRY' ENTERED AT 16:26:15 ON 13 NOV 2008
D STAT QUE L24

FILE 'ZCPLUS' ENTERED AT 16:26:26 ON 13 NOV 2008
D STAT QUE L25

FILE 'WPIX' ENTERED AT 16:26:43 ON 13 NOV 2008
D STAT QUE L33

FILE 'BEILSTEIN' ENTERED AT 16:26:53 ON 13 NOV 2008
D STAT QUE L28

FILE 'ZCPLUS, WPIX, BEILSTEIN' ENTERED AT 16:27:11 ON 13 NOV 2008
L48 13 DUP REM L25 L33 L28 (0 DUPLICATES REMOVED)
 ANSWER '1' FROM FILE ZCPLUS
 ANSWERS '2-5' FROM FILE WPIX
 ANSWERS '6-13' FROM FILE BEILSTEIN
D IBIB ABS HITSTR L48 1
D IALL HITSTR L48 2-5
D IDE ALLREF L48 6-13

FILE HOME

FILE ZCPLUS

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FILE COVERS 1907 - 13 Nov 2008 VOL 149 ISS 20
FILE LAST UPDATED: 12 Nov 2008 (20081112/ED)

ZCplus now includes complete International Patent Classification (IPC) reclassification data for the second quarter of 2008.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE REGISTRY

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 12 NOV 2008 HIGHEST RN 1072189-85-5

10/586494

DICTIONARY FILE UPDATES: 12 NOV 2008 HIGHEST RN 1072189-85-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH July 5, 2008.

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

FILE BEILSTEIN
FILE LAST UPDATED ON April 1, 2008

FILE COVERS 1771 TO 2008.
FILE CONTAINS 10,322,808 SUBSTANCES

>>> PLEASE NOTE: Reaction Data and substance data are stored in separate documents and can not be searched together in one query. Reaction data for BEILSTEIN compounds may be displayed immediately with the display codes PRE (preparations) and REA (reactions). A substance answer set retrieved after the search for a chemical name, a compounds with available reaction information by combining with PRE/FA, REA/FA or more generally with RX/FA. The BEILSTEIN Registry Number (BRN) is the link between a BEILSTEIN compound and belonging reactions. For more detailed reaction searches BRNs can be searched as reaction partner BRNs Reactant BRN (RX.RBRN) or Product BRN (RX.PBRN).<<<

>>> FOR SEARCHING PREPARATIONS SEE HELP PRE <<<

* PLEASE NOTE THAT THERE ARE NO FORMATS FREE OF COST.
* SET NOTICE FEATURE: THE COST ESTIMATES CALCULATED FOR SET NOTICE
* ARE BASED ON THE HIGHEST PRICE CATEGORY. THEREFORE; THESE
* ESTIMATES MAY NOT REFLECT THE ACTUAL COSTS.
* FOR PRICE INFORMATION SEE HELP COST

>>> Price change as of January 1st, 2008: Connect Time and Structure
Search fees re-introduced. See NEWS and HELP COST <<<

FILE WPIX
FILE LAST UPDATED: 12 NOV 2008 <20081112/UP>
MOST RECENT UPDATE: 200873 <200873/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE
>>> Now containing more than 1.2 million chemical structures in PCR <<

>>> IPC Reform backfile reclassifications have been loaded to end of September 2008. No update date (UP) has been created for the reclassified documents, but they can be identified by 20060101/UPIC, and 20061231/UPIC, 20070601/UPIC, 20071001/UPIC, 20071130/UPIC, 20080401/UPIC, 20080701/UPIC and 20081001/UPIC.
ECLA reclassifications to mid August and US national classification mid September 2008 have also been loaded. Update dates 20080401,

10/586494

20080701 and 20081001/UPEC and /UPNC have been assigned to these. <<

FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
PLEASE VISIT:

http://www.stn-international.de/training_center/patents/stn_guide.pdf

FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
<http://scientific.thomsonreuters.com/support/patents/coverage/latestupdate>

EXPLORE DERWENT WORLD PATENTS INDEX IN STN ANAVIST, VERSION 2.0:
http://www.stn-international.com/archive/presentations/DWPINAvaVist2_0608.p

>>> HELP for European Patent Classifications see HELP ECLA, HELP ICO <<<

FILE MEDLINE

FILE LAST UPDATED: 12 Nov 2008 (20081112/UP). FILE COVERS 1949 TO DATE.

MEDLINE has been updated with the National Library of Medicine's revised 2008 MeSH terms. See HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

See HELP RANGE before carrying out any RANGE search.

MEDLINE Accession Numbers (ANs) for records from 1950-1977 have been converted from 8 to 10 digits. Searches using an 8 or 10 digit AN will retrieve the same record. The 10-digit ANs can be expanded, searched, and displayed in all records from 1949 to the present.

FILE EMBASE

FILE COVERS 1974 TO 13 Nov 2008 (20081113/ED)

EMBASE was reloaded on March 30, 2008.

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

Beginning January 2008, Elsevier will no longer provide EMTREE codes as part of the EMTREE thesaurus in EMBASE. Please update your current-awareness alerts (SDIs) if they contain EMTREE codes.

For further assistance, please contact your local helpdesk.

FILE BIOSIS

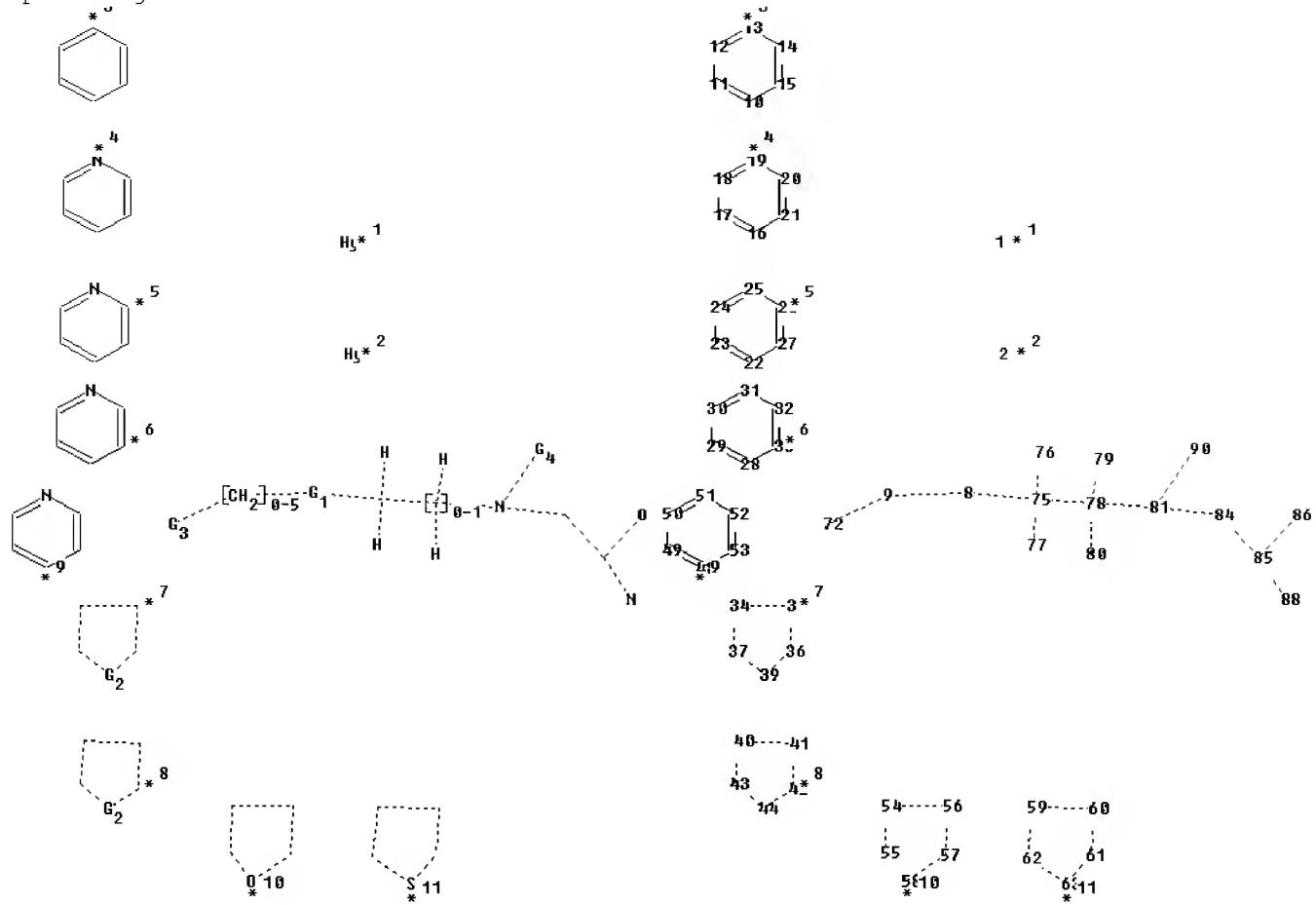
FILE COVERS 1926 TO DATE.

CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNS) PRESENT FROM JANUARY 1926 TO DATE.

RECORDS LAST ADDED: 13 November 2008 (20081113/ED)

BIOSIS has been augmented with 1.8 million archival records from 1926 through 1968. These records have been re-indexed to match current BIOSIS indexing.

Uploading L7.str



chain nodes :

1 2 8 9 72 75 76 77 78 79 80 81 85 86 90

ring nodes :

10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30

31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55

56 57 58

59 60 61 62 63

ring/chain nodes :

84 88

chain bonds :

8-9 8-75 9-72 75-76 75-77 75-78 78-79 78-80 78-81 81-84 81-90 84-85 85-

86

85-88

ring bonds :

10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-21 17-18 18-19 19-20 20-21

22-23 22-27 23-24 24-25 25-26 26-27 28-29 28-33 29-30 30-31 31-32 32-33

34-35 34-37

35-36 36-39 37-39 40-41 40-43 41-42 42-44 43-44 48-49 48-53 49-50 50-51

51-52 52-53

54-55 54-56 55-58 56-57 57-58 59-60 59-62 60-61 61-63 62-63

exact/norm bonds :

8-9 8-75 9-72 34-35 34-37 35-36 36-39 37-39 40-41 40-43 41-42 42-44 43-

44

54-55 54-56 55-58 56-57 57-58 59-60 59-62 60-61 61-63 62-63 75-76 75-77

75-78 78-79

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78-80 78-81 81-84 81-90 84-85 85-86 85-88

normalized bonds :

10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-21 17-18 18-19 19-20 20-21
22-23 22-27 23-24 24-25 25-26 26-27 28-29 28-33 29-30 30-31 31-32 32-33
48-49 48-53
49-50 50-51 51-52 52-53

G1:[*1], [*2]

G2:O, S

G3:[*3], [*4], [*5], [*6], [*7], [*8], [*9], [*10], [*11]

G4:H, Cb, Ak

Connectivity :

85:3 E exact RC ring/chain 86:1 E exact RC ring/chain

Match level :

1:Atom 2:Atom 8:CLASS 9:CLASS 10:Atom 11:Atom 12:Atom 13:Atom 14:Atom
15:Atom
16:Atom 17:Atom 18:Atom 19:Atom 20:Atom 21:Atom 22:Atom 23:Atom 24:Atom
25:Atom 26:Atom
27:Atom 28:Atom 29:Atom 30:Atom 31:Atom 32:Atom 33:Atom 34:Atom 35:Atom
36:Atom 37:Atom
39:Atom 40:Atom 41:Atom 42:Atom 43:Atom 44:Atom 48:Atom 49:Atom 50:Atom
51:Atom 52:Atom
53:Atom 54:Atom 55:Atom 56:Atom 57:Atom 58:Atom 59:Atom 60:Atom 61:Atom
62:Atom 63:Atom
72:CLASS 75:CLASS 76:CLASS 77:CLASS 78:CLASS 79:CLASS 80:CLASS 81:CLASS
84:CLASS 85:CLASS
86:CLASS 88:CLASS 90:CLASS

Generic attributes :

1:

Saturation : Unsaturated
Type of Ring System : Polycyclic

2:

Saturation : Unsaturated
Type of Ring System : Polycyclic

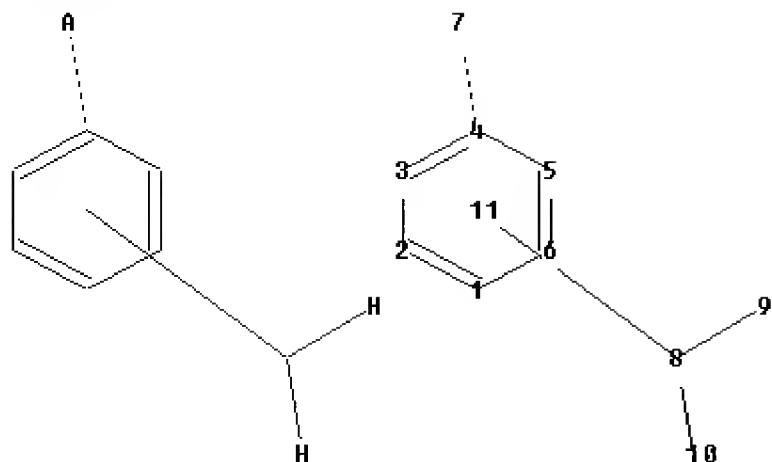
Element Count :

Node 1: Limited
O,O1

Node 2: Limited
S,S1

Uploading L11.str

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chain nodes :

8 9 10

ring nodes :

1 2 3 4 5 6 7

chain bonds :

8-9 8-10

ring bonds :

1-2 1-6 2-3 3-4 4-5 4-7 5-6

exact/norm bonds :

4-7

exact bonds :

8-9 8-10

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:CLASS 9:CLASS 10:CLASS
11:CLASS

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